UNITED STATES DISTRICT COURT
DISTRICT OF SOUTH CAROLINA
CHARLESTON DIVISION

SUZANNE Q. LITTLE, individually and as Personal Representative of the Estate of SAMUEL MARTIN LITTLE, deceased,

Plaintiff(s),

vs. CIVIL ACTION NO. 2:98-1879-23

BROWN & WILLIAMSON TOBACCO CORPORATION, individually and as successor by merger to the AMERICAN TOBACCO COMPANY, and R.J. REYNOLDS TOBACCO COMPANY,

Defendant(s).

VOLUME II

DEPOSITION OF: RUSSELL A. HARLEY, M.D.

DATE: TUESDAY, MAY 23, 2000

TIME: 9:00 a.m.

LOCATION: Medical University of South Carolina
171 Ashley Avenue, Room HD274
Charleston, South Carolina

TAKEN BY: Attorneys for the Defendant(s)

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(INDEX AT REAR OF TRANSCRIPT)

STIPULATION: It is stipulated by and among Counsel that this deposition is being taken in accordance with the Federal Rules of Civil Procedure; and that the deponent does not waive reading and signing of this deposition.

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RUSSELL A. HARLEY, M.D., being first duly sworn, testified as follows:

EXAMINATION

BY MS. SCHMAHL:

Q. Good morning, Dr. Harley. My name is Robin Schmahl. We met during the first day of your deposition. Do you understand that this is a continuation of your deposition from April 17?

A. I do.

Q. And you're still under oath, and the same rules apply as to the first day of your deposition.

A. I understand.

Q. Since the day of your last deposition, have you discussed this case with Plaintiffs' attorneys?

A. Only briefly, not to any really great extent. They sent me copies of Dr. Barsky's deposition and said they were coming and would I please have a look at those, and that's about it.

Q. Okay. And did you have a look at Dr. Barsky's

deposition?

A. Yes.

Q. Did you draw any conclusions from your review of his deposition?

A. Yes.

Q. And what were those conclusions?

A. I was, of course, impressed by his CV, yet again. He's a very accomplished researcher. I was a little surprised at the number of bronchioloalveolar carcinomas that he finds in his studies in Southern California, in which they were extraordinarily common compared with most other studies.

I noted the photographs that he had taken of areas of the tumor in Mr. Little's case, which had bronchioloalveolar features. And I also observed the photographs that he had taken of other given -- that is, known bronchioloalveolar carcinomas.

Basically, my impression of the photographs that he's taken in Mr. Little's case are that these are probably of areas that I remember seeing, small -- actually, one small area, that I did not think, if I'm correct, I did not think was cancer. I thought this was atypical hyperplasia and not part of the tumor.

There's a lot of interesting science in his deposition, and so I enjoyed reading it from that

232

standpoint.
Q. When you examined the photographs that Dr. Barsky had made, did you see BAC in those photographs or what would be consistent with BAC?
A. I saw something that, based on those photographs, one could say was BAC.
Q. Did you see Clara cells in any of those photographs?
A. Possibly so. I remember seeing what I thought were hyperplastic type 2 cells.
As I said, when I looked at these in the original, I saw a small focus of what I thought was atypical bronchioloalveolar hyperplasia that I did not think was cancer. I have looked at these slides pretty carefully, so I thought that the area that he photographed must have been from that little area that I remembered.
The hyperplastic cells may contain some Clara cells; they may be type 2 cells. I really couldn't say from looking at the photographs.
Q. And either Clara cells or type 2 cells are suggestive of BAC; is that correct?
A. They are the malignant cell in BAC, yes.
Q. Were you asked to review or pay any special emphasis to certain portions of Dr. Barsky's deposition or deposition exhibits?

233

A. No, I was just asked to review it and form impressions.
Q. What, after reviewing it, what was your ultimate impression?
A. That Dr. Barsky believes this is a bronchioloalveolar carcinoma; that he believes that bronchioloalveolar carcinomas, even though they are increasing in the general population, are not necessarily related to cigarette smoking, or at least not as closely as the other common lung cancers. And as I've said, he thinks these are much commoner cancers than most other people.
If you can hearken back to the two summaries that I gave you of the types of cancers that we think are being -- that we are seeing here in Charleston, the bronchioloalveolar carcinomas were relatively uncommon; whereas, he finds them, according to his work, in about 24 percent of the lung cancer population, which is the highest I've seen anywhere.
So he seems to be at one end of the spectrum and we seem to be toward the other, and I don't know exactly how to explain this rather extraordinary number of BACs in his population.
Q. Did you review in his deposition -- or reviewing the exhibits, did Dr. Barsky reach any conclusions that

234

you thought could not be supported by medical science?
A. The big one, I think, is that the portion of this that he calls bronchioloalveolar carcinoma, I think many of us would not. I think many of us would say it's atypical hyperplasia.
I can't really speak for other pathologists or other lung pathologists, and this is something that would require a pathologist having that slide in his hand, under his own microscope, to come to a firm conclusion.
Q. Okay. But absent having that slide, under your microscope, you could not come to a firm conclusion, one way or another, whether Dr. Barsky correctly identified that as being BAC rather than atypical hyperplasia; is that correct?
A. That's correct. And I think that's one of the linchpins of this whole thing. This particular tumor behaved in some ways like a bronchioloalveolar carcinoma, in that it tended to spread through the lungs before it went to other places.
On the other hand, it never looked like a bronchioloalveolar carcinoma, and I'm not the only one who looked at it; there were other highly-respected lung pathologists who also looked at it, I believe.
I think Dr. Roggli looked at it; he's very good. And, I think, Dr. Sam Hammar looked at it; he's also very

235

good. And I don't believe either one of them thought this was a BAC. And they had the same slides that I had and that Dr. Barsky had. So you've got four people looking at the same material and coming to different conclusions.
Dr. Barsky has sort of specialized in BACs among the lung cancers. Much of his work has to do with breast cancer and with basic mechanisms of behavior of cancer, invasion of cancer, and protection the body throws up against invasion.
He -- I don't think he over-reads bronchioloalveolar carcinoma ordinarily. His study in which he found large numbers of BACs, especially in women in California, I believe is probably true in that study in that population.
But I think, in this case, the tiny area that he's looking at is a response of the lung to injury, that is, to the adjacent large cell cancer, and to the radiation and the chemotherapy that were given, that this, in other words, happened after the fact and does not indicate that this particular cancer sprang from the BAC. Nevertheless, I see his viewpoint.
Q. Dr. Harley, can you match the photomicrograph up to the pathology sample? Is it identified which pathology sample the photomicrograph comes from?
A. I don't believe he said exactly which one, but I

236

do remember seeing an area of something that I thought was atypical hyperplasia in one of those slides.
Q. Let me ask --
A. Now, this is really going pretty far out, but I think it was slide 7, something or other 7, I think, but that's pushing my memory a little far.
Q. Okay. Would that be photomicrograph 7?
A. No, I'm talking about the glass slides. I'm sorry. I'm not talking about photomicrographs; I'm speaking of the glass slides, themselves.
Q. Well, let me ask you, if Dr. Barsky took the photomicrograph from the pathology sample that was collected on December 18th, 1995, the pathology materials on those glass slides would not have any radiation reaction; is that correct?
A. I would have to go back and look at the dates on all this again, it's a little blurry, but if he took photographs before chemotherapy and radiation, then they would not have chemotherapy and radiation changes.
Q. So if the photomicrographs that Dr. Barsky took show what he calls BAC and you think might be atypical hyperplasia, and that photograph was taken before the radiation and chemotherapy, what Dr. Barsky is seeing is not a response to radiation or chemotherapy; is that correct?

237

A. That's correct.
Q. And sitting here today, is it your belief that the area that you looked at that had hyperplasia was a post-radiation, post-chemotherapy pathology slide?
A. That's what I remembered, but it's been an awful long time since I looked at these. I do remember seeing some atypical -- some reaction that I thought was atypical bronchioloalveolar response, and I think I remember seeing it adjacent to cancer. And I was assuming that this was in the treated cancer, because that's what most of what we saw and took pictures of.
Q. Is it not correct that what Dr. Barsky noted in his photomicrographs is more significant if it comes from an area of cancer that has not been treated with either chemotherapy or radiation?
A. That's correct.
Q. Since your last deposition, have you talked to Dr. Reed about Mr. Little or this case?
A. No, I have not.
Q. Have you, at any time, talked to Dr. Reed about Mr. Little or this case, outside of the context of treating Mr. Little?
A. I do remember at one point, saying -- asking her how her deposition went. And as I remember it, she made a face and said something about its being long.

238

Q. Any other discussions that you had with Dr. Reed?
A. No.
Q. Exchanged any e-mails with her or exchanged any correspondence with her regarding Mr. Little or this case?
A. I don't think so.
Q. How about Dr. Hammar; have you discussed Mr. Little or this litigation with him?
A. I don't believe so. I don't -- I saw him in New Orleans, and I don't really remember what we talked about other than an upcoming meeting, so I don't think we talked about this.
Q. Dr. Victor Roggli?
A. If I said anything to him or he said anything to me about the case, it was awfully short and tangential. We also talked at the New Orleans meeting about the possibility of doing a study on BAC which we are going to have to modify somewhat. And in that context, we probably did mention this case. I don't remember anything specific about it, though.
Q. Have you discussed this case with anyone else other than the individuals that we have already talked about?
A. I don't believe so.
Q. Since your last deposition, have you reviewed

239

any medical records regarding Martin Little?
A. Only Dr. Barsky's deposition.
Q. Have you reviewed any medical articles or texts in preparation for this litigation?
A. No.
Q. Have you done a MedLine search on any topics with regard to this litigation?
A. I looked up Dr. Mark Green's article, which I believe was in the Journal of Clinical Oncology some years ago --
Q. And what --
A. -- which is a reference that Dr. Barsky had in his deposition. I looked up the abstract and found it to be fairly general, saying that there seemed to be an increase in BAC.
Q. Okay. And why, in particular, did you look up Dr. Green's BAC article?
A. Because I see him with some frequency, and I thought that if the subject of BAC in general should come up, that it would sort of be a courtesy for me to have read his article.
Q. Other than --
A. And because I respect his opinion.
Q. Other than Dr. Barsky's deposition, have you read any other of the depositions that have been taken in

240

this case?
A. Yes, I think I referred to those in my previous half of this deposition, and I think I have looked through all of them that were sent to me, at some point.
Q. Okay. And those would be depositions that we had identified at your last --
A. I believe so.
Q. -- deposition by name.
Any others? Have you received any others since the date of your last deposition?
A. No, I don't think so.
Q. And have you reviewed the expert reports of any of the Defendants' experts in this case?
A. I don't think so. Could you clarify that further, an example?
Q. You prepared an expert report --
A. Right.
Q. -- for this case. Our expert witnesses also prepared expert reports for this case. Have you reviewed any of those expert reports that lay out a summary of the Defendants' witnesses' opinions?
A. Only Dr. Barsky's.
Q. Okay. Dr. Harley, when we adjourned your last deposition, we were in the process of going through the photomicrograph slides that you made, and I believe we

241

left off with slide 18-3?
A. I have it here.
Q. Is there a way for us to get the carousel set up without --
A. We can -- this sort of thing, I can do.
MS. SCHMAHL: Let's take a quick break and we can get the room set up and get back to it.
(A recess transpired.)
BY MS. SCHMAHL:
Q. Dr. Harley, is what we have on the slide projector, is that 18-2 or 18-3?
A. This is 18-2.
Q. I believe that we have talked about 18-2 during your last deposition, so could we go forward to 18-3, unless there's something else you need to point out for me.
A. Well, just for the sake of clarity and to make sure this comes out the same way, because it is confusing, this is 18-2. And as it now appears on the screen, the tumor is a strip of cells running from the bottom right center to the upper left corner. And there is tumor necrosis in the lower left corner of the slide, which would be the key feature that a pathologist would see.
Q. All right.
MS. SCHMAHL: Can we go off the record

242

again?
(Off-the-record conference.)
BY MS. SCHMAHL:
Q. Dr. Harley, for the sake of clarity, and so that we all know how to look at these slides when we put them in our carousels, you put the slides in the carousel with the label that shows the pathology specimen number at the top, correct?
A. Right. So that if one is looking at the slide and reading the number and the name, it goes in just like that; that name is at the top and facing the back of the carousel.
Q. Thank you.
We left off last time discussing slide 18-3. Would you bring that slide up on the carousel, please?
A. (Complying)
Q. Slide 18-3 is a photograph taken at medium power; is that correct?
A. Correct.
Q. Please describe the histological features of 18-3.
A. At the upper right corner is a vessel, a blood vessel, which I think is a pulmonary vein, because there's a connective septum running into it.
In the center of the slide, more or less,

243

there's a blood vessel containing red blood cells. And just adjacent to that and below it to the left, at 7:00, there's an enlarged air space.
There are some other similar enlarged air spaces in the photograph. The enlarged air spaces are suggestive of a very mild degree of emphysema. They are not absolutely diagnostic of it, in that this could be local hyperinflation and artifact, but the location near the center of the acinous, which is where the largest air space is, and the overall appearance, is suggestive of a slight degree of centrilobular emphysema.
I find centrilobular emphysema, to some degree, in the lungs of most chronic cigarette smokers and -- so I suppose the reason I took this, was that I was thinking about tobacco smoking, wondering if there were any emphysema there.
There's another feature suggestive of emphysema. If one looks at the enlarged air space, directly above it is another small pulmonary artery, and to the left of that is a space that has a portion of tissue which seems to be floating free; it's not attached anywhere.
The lack of attachment suggests that there might be destruction of tissue, which is the hallmark of emphysema; that is, holes in the lung. Nevertheless, this is minimal emphysema, if it really is emphysema at all.

244

Q. Okay. Now, you said that it could be hyperinflation.
A. Right.
Q. What are some of the things that can cause hyperinflation?
A. In material like this, it's been handled by pathologists who have been looking at it, cutting it, and pulling it, and sometimes it's an artifact. The air is trapped there, and the air spaces away from the area of hyperinflation are relatively compressed. One sees that at the upper right corner, and to some extent, the lower left corner.
So if those, the ones at the lower left and upper right corners collapse, then that would pull open the ones in the middle. So it could just be an artifact.
Hyperinflation, in real life, is caused by intentionally holding one's breath or by obstruction of an airway from a mucus plug or from asthma. In this case, it has little significance.
Q. Okay. And would it be fair to say that, based on what you see in slide 18-3, you couldn't make a clinical diagnosis of emphysema?
A. No, I wouldn't.
Q. Is there anything in slide 18-3 that would be indicative of cancer type?

245

A. No.
Q. Does 18-3 show any active cancer?
A. No.
Q. Does it show any cancer at all?
A. Not a bit.
Q. Does 18-3 support your opinions?
A. No, neither one way, nor the other. It may indicate a small degree of histologic emphysema, which differs from what you refer to as clinical emphysema, which is symptomatic and requires destruction of a great deal of lung tissue before one knows it's there.
Q. But there's nothing inside 18-3 that would allow you to testify, with a reasonable degree of medical certainty, that Mr. Little, in fact, had emphysema; is that correct?
A. No, I don't believe he did.
Q. Do you intend to show slide 18-3 to the jury?
A. I don't think so.
Q. Could you please put 18-4 in the carousel?
A. (Complying)
Q. Now, slide 18-4, that actually corresponds to Figure 4 on Exhibit 4. You had provided for us some color photographs of the slides; is that correct?
A. Correct.
Q. Does 18-4 show the same field as 18-3?

246

A. I don't think so. I need to go back and look.
It's possible that this is in the corner of 18-3. I can't tell for sure from this distance.
Q. 18-4 was taken at a higher magnification than 18-3; is that correct?
A. Correct.
Q. Do you know what the power of the lens was that you used on 18-4?
A. It looks like an objective lens of about 25X.
Q. Okay. Can you please describe for us the histological features of 18-4?
A. This is, again, the center of an acinous somewhere in the lung, and a pulmonary artery is present at the lower left portion of the slide. The center of the slide contains air spaces which have a number of large macrophages with abundant finely granular brown cytoplasm. This is at the center of an acinous, because it's adjacent to the pulmonary artery.
And the presence of the brown macrophages is suggestive of so-called respiratory bronchiolitis, which is characteristically seen in cigarette smokers. So, again, this would be an example of something one might find in a cigarette smoker which, I think everybody agrees, Mr. Little was. It really serves no great purpose other than to suggest that indeed he was what he was, was

247

a cigarette smoker.
Q. Is there anything in 18-4 that is indicative of cancer?
A. No.
Q. Then I take it, there's nothing in 18-4 that is indicative of the cell type of cancer.
A. Correct.
Q. Does 18-4 support your opinion with respect to cell type in any way?
A. No.
Q. Does slide 18-4 show signs of emphysema?
A. I don't believe so.
Q. Does -- is there anything in slide 18-4 that you are relying upon in forming your opinion, either on causation or cell type?
A. No. It's a reminder that Mr. Little is a cigarette smoker, but it doesn't prove it. These cells or similar cells can be found in other conditions, and I think it's a given that he smoked cigarettes, in any case, so really not.
Q. Do you intend to show slide 18-4 to the jury?
A. I don't think so, unless the conversation gets away from cancer and is then into tobacco smoking, in general, and I would hope that it would be more focused than that.

248

Q. So this, to the extent you showed slide 18-4, it's a type of photo that would just provide background information; is that correct?
A. Correct. It's a talking point, if one wanted to talk about lymphocytes, or macrophages, or alveoli, it could be used for that, but in talking about cancer directly, it shows no cancer.
Q. Could you bring up, please, slide 18-5?
A. (Complying)
Q. 18-5 is a fairly high-powered magnification, correct?
A. Correct.
Q. Is that a 40X lens?
A. I believe so.
Q. What field does slide 18-5 show? Is it the same as 18-4?
A. There's a -- let me answer that indirectly. There's a large macrophage in the center, which is fairly characteristic of two nuclei, and another small macrophage adjacent to it, and a small degenerating cell adjacent to that. If we can find that same thing, then I can answer your question.
I don't believe so. It's the same general process, so it could be.
Q. Is there anything in slide 18-5 that is

249

indicative of cancer?
A. No.
Q. Nothing in 18-5 that is indicative of cell type?
A. No, there's not.
Q. Does anything in 18-5 support your opinion with respect to cell type?
A. No.
Q. Would you please describe the histological features of 18-5?
A. It's a high power of lung somewhere containing brown macrophages, including a few small black specs of carbon dust. It is typical of what one might see in respiratory bronchiolitis, as we've mentioned. There's another macrophage with more black dust off to the side.
So this could be something found in a cigarette smoker's lung, although this degree might be seen in other conditions.
Q. Could this degree be seen in lungs of nonsmokers?
A. This accumulation of brown macrophages can occur in a whole host of conditions, but numerous centrilobular or centriacinar collections of these --
COURT REPORTER: Or what; I'm sorry?
THE DEPONENT: Centrilobular or centriacinar, a-c-i-n-a-r, are found much, much more commonly in

250

cigarette smokers.
BY MS. SCHMAHL:
Q. Does slide 18-5 show any evidence of emphysema?
A. No.
Q. Does it show any evidence of asthma?
A. No.
Q. Does slide 18-5 support your opinion with respect to cell type at all?
A. No, it does not.
Q. Does it support your opinion with respect to causation at all?
A. No, except that it's fairly characteristic of one of the changes seen in cigarette smokers.
Q. Do you intend to --
A. But, again, I think we've given the fact that Mr. Little was a cigarette smoker, so this really is unnecessary.
Q. Okay. So macrophages would tend to show that Mr. Little was a cigarette smoker; is that correct?
A. Right; whereas, his history is, I think, clear-cut, so this is an unnecessary point.
Q. Let's just discuss -- strike that.
Do you intend to show slide 18-5 to the jury?
A. I don't believe so, unless that kind of conversation is called for, for some reason. If someone

251

wants to talk about macrophages, we have some great macrophages here.
Q. So both slides 18-4 and 18-5 show macrophages, right?
A. Right.
Q. And is it correct that macrophages encapsulate foreign materials that get into the lungs?
A. That's one of their many functions, yes.
Q. Some of the foreign materials that could be encapsulated by macrophages would be air pollution; is that right?
A. Correct.
Q. You've already mentioned carbon dust.
A. Right.
Q. Dirt that's breathed in?
A. That's correct, almost any particle that can get into the alveoli is taken up by macrophage.
Q. Asbestos?
A. Correct.
Q. Silica?
A. Yes.
Q. Tobacco smoke?
A. Yes.
Q. Marijuana smoke?
A. Yes.

252

Q. Is there anything else that you can think of that would be common respirable dust that may be encapsulated by macrophages?
A. I can think of lots of them, but just any particle that's less than about 10 microns can get into the alveoli, and nearly all of those would elicit a response by the macrophage, and it would tend to engulf it.
Q. How about substances that are found in aerosols, like deodorants, would that have a dust that would be respirable?
A. It could, yes.
Q. Colognes and other spray-on scents?
A. Most of those don't have particles. They have tiny droplets of liquid; whereas, a macrophage might respond to such material, you couldn't see it and couldn't -- you'd have to do a chemical test to see if the macrophage had engulfed it.
Q. Exhibit 7 --
A. May I turn this off?
Q. Oh, certainly.
A. It's making noise.
Q. You get the carousel; we'll get the lights.
(Off-the-record conference.)
BY MS. SCHMAHL:

253

Q. Dr. Harley, Exhibit 7 to your deposition is your chapter on tobacco which is published in Dail and Hammar's book, Pulmonary Pathology, Second Edition. Do you stand by what you wrote?
A. That's a good question. I wrote this a good many years ago, and I do change my mind from time to time. And this was a difficult chapter to write, because there was so much that could be written. It was hard to narrow it down for the purposes of a chapter in a pathology textbook, but in general, yes, I do.
Q. Okay. This chapter was published in 1994; is that correct?
A. That's okay with me; I can't remember.
Q. Is there anything that you disagree with today that is contained in your tobacco chapter?
A. Probably. A lot of this stuff changes from year to year. My perceptions of things having to do with lung pathology change all the time. So I wouldn't exclude the possibility of there's something in here that I changed my mind about. Offhand, I don't know of anything.
Q. All right. Well, let me ask you to turn to page 835, first sentence -- well, actually the first full sentence in the right-hand column.
A. Macrophages accumulate in great numbers?
Q. You wrote there, "Macrophages accumulate in great numbers and collect in the alveoli of respiratory bronchioles. Bronchoalveolar lavage produces roughly 10,000 macrophages per milliliter from non-smokers and 40,000 per milliliter from smokers," end quote. Do you still agree with that statement?

254

A. I gave a reference at the end of the next sentence, which is number 35. The reference is to an article by Brody and Craighead, who are excellent people, and I don't know what other studies of BALs are producing now.
As far as the differences between macrophages watched from the lungs of smokers versus nonsmokers, and obviously it would vary a whole lot, depending on how much a person smoked, how old he was, and other conditions.
But in general, I stand by it, in that the lungs of smokers do have a lot more macrophages than nonsmokers.
Q. Do you also stand by the fact that, irrespective of whether the patient is a smoker or nonsmoker, quote, macrophages accumulate in great numbers and collect in the alveoli of respiratory bronchioles, end quote?
A. What I was referring to there was that they accumulate in great numbers and especially in cigarette smokers. They accumulate in great numbers in response to particulate matter. And the more particulate matter there is, the more macrophages there are.

255

For instance, in blank lung disease, where the entire lung appears black to the naked eye, nearly all of those black particles of coal mine dust are in macrophages. So it doesn't matter what the particle is.
The pattern of respiratory bronchiolitis seen in cigarette smokers is fairly characteristic. I think this was originally described by, perhaps Dennis Niewohner.
COURT REPORTER: Diewohner?
THE DEPONENT: N-i-e-w-o-h-n-e-r, and Jerry Kleinerman. I know that Dr. Kleinerman was one of the people who described this. And they noted this characteristic lesion in lungs of -- from forensic autopsies.
The forensic population, in addition to including lots of drug abuse and so forth, includes lots of cigarette smokers, and the lungs, in general, are cut without inflating them; whereas, in an academic center, where people are doing lung pathology, they tend to inflate the lungs with formalin. Inflation actually washes a lot of the macrophages out. So the forensic material shows a lot more of these.
And I think most of us in the lung pathology had not paid enough attention to this lesion, because we were looking at the lungs fixed the

256

proper way; whereas, the improper way actually shows us a lot better. And so --
BY MS. SCHMAHL:
Q. But my question is, do you agree or disagree that smokers and nonsmokers have macrophages?
A. Obviously, all have macrophages, but I wanted to defend the lesion of respiratory bronchiolitis. I think it's an important pathologic lesion; whereas, it's not an absolutely diagnostic, not apathic pneumonic lesion of cigarette smokers. It is quite characteristic. And I think in moderately heavy active smokers, it's always seen.
Q. Okay. Are macrophages found in the alveoli of both smokers and nonsmokers?
A. Always, yes.
Q. Now, you testified during Day One of your deposition that, quote, brown macrophages occur in a lot of conditions if the macrophages have been busy eating things, correct?
A. Correct.
Q. So brown pigmented macrophages occur from substances other than tobacco smoke; is that correct?
A. That's correct.
Q. And do you also agree that as macrophages age, their color tends to become brown due to an endogenous

257

pigmentation?
A. Yes.
Q. Do most or all macrophages turn brown as they age?
A. I would say, yes, but it depends on what they've been doing. If they have been phagocytosing, if they have been eating a lot of foreign material, they do turn brown. If they have not, they perhaps might not. Brown pigment wouldn't accumulate in some macrophages.
Q. What is the life cycle of a macrophage; how long do they live?
A. You know, I'm not sure. They're not all that long-lived. I used to know this when I was a medical student. They begin life in the bone marrow. They circulate in the blood as monocytes.
They leave the blood and -- they may leave the blood and wander off in the tissues where they are termed histiocytes. They -- certain ones will accumulate in certain organs where they continue to differentiate, so that macrophages found in the lung may produce different enzymes than the ones found in the peritoneum. And they belong to a large family of phagocytic cells which, in general, as I've said, begin life in the brown marrow.
When one looks at bronchioloalveolar lavage, there are some small macrophages and there are big

258

macrophages; there are non-pigmented ones, and there are pigmented ones. And the general concept, which I think is true, is that the small nonpigmented ones are younger; they've just gotten there. And the big, old, fat brown ones are the old ones, and then one sees them in the process of dying or crawling off to their elephant's graveyard or wherever they go.
So there is a life cycle that's seen there that takes place in the order of weeks.
Q. So --
A. So a macrophage would not live to be six months old.
Q. Okay.
A. It would be weeks.
Q. And what happens to the material that's been absorbed by a macrophage if the life cycle of a macrophage is only -- is less than six months?
A. If it's in the alveolus, when it eats a foreign particle, there are three things that can happen to it. Number one, it can stay there and it can die there, in which case the foreign material would be picked up by another macrophage and held.
Alternatively, the macrophage, with its foreign particle, could move up to an airway where cilia can be found and could ride along on the mucous ciliary escalator

259

out of the lung, up into the trachea, and then be swallowed or coughed out.
And the third possibility would be for the macrophage to get into the interstitium into the lymphatic system and go to a regional lymph node where it might stay and die and deposit its particle.
Q. Do you have an opinion on how long foreign matter stays in the lungs in a macrophage before it's either carried out of the lungs or deposited into the lung system?
A. The topic that you're getting into there is alveoli clearance, which is a fairly mysterious topic. When particles are inhaled, most of them either are stopped by the nose or they land on the airways somewhere, and those are cleared in about a day. The ones that get into the alveoli are cleared very slowly, if at all, and they may stay for years.
In the case, for instance, of a coal miner, they may stay there for years and years until the coal miner develops heart failure, some pulmonary edema, and begins to wash his lungs out. He may then start coughing up great quantities of black material that's been there all his life.
But in general, it stays for months to years, and oftentimes for the lifetime of the person, depending

260

on how easily digested it is.
Q. Okay. Are you able to determine how old a macrophage is by looking at it under a microscope?
A. Just in general. As I say, the big brown ones are older than the young white ones, pink ones.
Q. If macrophages turn brown as they age, and if macrophages can be brown from swallowing substances other than tobacco smoke, then can you tell by looking at a macrophage under the microscope what substance that macrophage has swallowed?
A. Sometimes. The macrophages that we've showed here today are brown because they contain lipofuscin, which, as you've mentioned, is an endogenous pigment; it's made as the macrophage ages. And I can stain that, although not specifically, it could be analyzed chemically, and I can say there's lipofuscin.
If I really worked on it, I could probably say how old a macrophage was, more or less. Other things that turn macrophages brown, though, for instance, are hemosiderin, which is iron pigment, and that's usually lumpy, and there's a stain for it, so I can say that's an iron containing macrophage or brown foreign material such as iron ore, and I can tell what that is by looking at it, more or less.
Q. But without doing --

261

A. But --
Q. -- doing special stains or special testing, just with the slides that you've shown me, 18-4, 18-5?
A. All I could say is that looks like lipofuscin, and it's got a few little black particles. I could not tell you whether there's cigarette smoke in that or whether the little black particles came from tires or dirt in the air or exactly what.
Q. Okay. So if you had a pathology slide from an anonymous patient, and it had the features that we saw in 18-4 or 18-5, could you simply, by examining that slide under a microscope, tell whether the patient was a smoker or nonsmoker?
A. I could give you some rough percentage, like the chances are 80 percent this person is a smoker and -- or maybe 95 percent or maybe 95 percent that he's not, and I can be in the ballpark, but I can't be precise. And, of course, it depends on who took the slide and where it's from.
Q. I'm talking about what we saw in 18-4 and 18-5.
A. No, from looking at that, I couldn't tell you for sure that that was a cigarette smoker. In fact, I wouldn't even get much over 60 percent in one like that.
Q. So your opinion that those are smoker's macrophages, is it fair to say, is based in part on the

262

fact that you know Mr. Little was a smoker?
A. Oh, yeah, I'm pretty sure that's a smoker's macrophage, because they came from Mr. Little, and he was a smoker.
Q. Okay.
A. But whether those are a typical smoker's macrophages, you know, if you just took those from some unknown lung and gave them to me and said -- gave me that picture and said, Is that a smoker, I couldn't say.
Q. Now, lung cancer is caused by cellular mutations, correct?
A. Yes.
Q. Smoker macrophages don't cause lung cancer, do they?
A. That could be a very complex question, but basically, no.
Q. Smoker's macrophages are not necessary or sufficient for lung cancer; is that correct?
A. That's correct.
Q. The presence of smoker's macrophages does not demonstrate that cancer mutations have taken place; is that correct?
A. Correct.
Q. And the pathologist wouldn't make a diagnosis of cancer based simply on the presence of what you called

263

smoker's macrophages?
A. Oh, no, not at all.
Q. Would you agree that the presence of smoker's macrophages is not suggestive of the cell type of a cancer?
A. Absolutely.
Q. If there's no dispute that Mr. Little was a smoker, then the presence of these smoker's macrophages, does it have any relevance to your opinion?
A. Not really.
Q. Is your causation opinion dependent in any way on your finding of smoker's macrophages?
A. No.
Q. Doctor, if we could, let's switch gears a little bit to emphysema. Do you contend that Mr. Little had emphysema?
A. No. I would say that the photograph I took might show a very minimal histologic degree of it, but I would never attempt to publish that in a textbook as a picture of emphysema.
It is suggestive, but even if it were absolutely diagnostic of a small degree of emphysema, it would not suggest that Mr. Little had clinical emphysema or any serious degree of it. So from what I have seen, I don't see any evidence that he has clinical disease emphysema.

264

Q. Do you intend to offer any opinion whatsoever on emphysema?
A. No.
Q. Do you intend to offer any opinion that Mr. Little may have had a very mild case of emphysema?
A. No, unless I'm pinned against the wall.
Q. That won't be by me.
Dr. Harley, I'd like to discuss with you in a little bit greater detail your expert report which has been introduced into evidence as Exhibit 6.
MS. SCHMAHL: Let's take a break.
(A recess transpired.)
BY MS. SCHMAHL:
Q. Dr. Harley, is there anything in Exhibit 6 that you no longer agree with?
A. I don't believe so.
Q. Is Exhibit 6 a complete statement of your opinions regarding cell type and causation?
A. As regards Mr. Little, I think it's a pretty accurate summary of what I thought, think.
Q. Regarding both, cell type and causation?
A. That tobacco causes most lung cancer, in general, that there are other causes.
Q. Is Exhibit 6 an accurate statement of your opinions?

265

A. I think so.
Q. According to paragraph 1 of your report, there on the first page, you received three categories of materials from Plaintiffs' counsel; is that correct?
A. Correct.
Q. You received medical records from MUSC?
A. I believe I did. I think that Ness, Motley sent me copies of medical records, and I think I have them there in those big black notebooks somewhere.
Q. Those six black binders that are at the end of the room?
A. Correct.
Q. And Plaintiffs' attorneys, according to paragraph 1, also sent you a report by Dr. Victor Roggli?
A. Correct.
Q. Which contains his expert opinions on Martin Little; is that correct?
A. Right.
Q. And the third category of materials that you received are histopathological slides.
A. Correct.
Q. How much time did you spend reviewing Mr. Little's medical records before drafting Exhibit 6?
A. About two and a half hours, I think.
Q. Did you review all of his medical records or

266

just some of his more recent medical records?
A. I probably looked through nearly all of them, but I'm sure I didn't read them all in great detail.
Q. Did you review any of the x-ray films or CT scans from Mr. Little?
A. No, only the reports.
Q. Did you review all of the x-ray reports and CT scan reports?
A. Like the rest of the medical records, probably not in any detail.
Q. What information in the medical records would have caused you to have reviewed a specific medical record in more detail?
A. Well, I would have started off wanting to get a general picture, an overall picture of what had happened to Mr. Little, what his medical history was. And then once I had an idea of that, I'd want to look through the medical records and see if there's anything that caught my eye that would add to that, that I didn't know already.
Q. What sort of things would catch your eye that would be significant for your opinions?
A. I'd have to look through it and see, but in this case, the course of the disease, x-rays that showed other lesions. It seemed to me that he had some granulomas and so forth in his lungs, some of which were not explained,

267

any evidence that he had tumor elsewhere in his body.
The -- for instance, he had a CT of his head that showed changes in the brain that were thought to be caused by localized arteriosclerosis, and I would include something like that, because, in somebody with lung cancer, and the CT of the brain shows an abnormality, there would be the question of whether there might be a metastasis there.
Q. And in this case, though, there was not a metastasis to the brain, correct?
A. Correct.
Q. Do you know whether you received a complete set of Mr. Little's medical records?
A. I don't know for sure, but considering the volume of material that I got, I would hope so.
Q. Have you ever met Mr. Little or his wife, Suzie Little?
A. I think, yes, that I met him at a church function at least once, maybe twice, but I don't remember him. And I do remember having met his wife once or twice, although I really don't know her, and I'm not certain I'd recognize her if she came in the room now.
Q. Did you ever discuss the litigation with Mr. Little or his wife?
A. No.

268

Q. Did you ever discuss any aspect of his treatment with Mr. Little or his wife?
A. No. I don't believe, when I met him, that I knew he had lung cancer.
Q. So this was just a casual social meeting, unrelated to any form of treatment or this litigation?
A. I believe it was a church Christmas dinner or something like that.
Q. How much time did you spend reviewing Dr. Roggli's expert report before you drafted Exhibit 6?
A. Probably a few minutes. It was not that long, it didn't take long to read it.
Q. Did you bring a copy of Dr. Roggli's expert report with you today?
A. I think so.
Q. Could you put your hands on that?
A. Probably. Let's see what I have here.
It's going to be harder than I thought. It's not here in this little packet.
Now, this is -- I'm sorry; this is his deposition, and there was a report, I think, of his, which is not the same as the deposition. I'm not sure exactly where that is right now.
Q. I guess my question is, that you're saying that you received a report by Dr. Victor Roggli dated September

269

16th, 1998, and we don't have a copy of any such report, to the best of my knowledge.
A. I had intended to bring everything that I had in this case here. I had it all stacked up in my office. I don't see it right on the top, so perhaps it's still there.
Q. Perhaps we could take a break then and get --
A. I'll go look and see if I can find it.
MS. SCHMAHL: Okay.
(A recess transpired.)
BY MS. SCHMAHL:
Q. Let me ask you if have you seen this record before; is that the expert report of Dr. Victor Roggli that you received, or would you need to check your office to be sure?
A. Didn't you say that I thought the report was from --
Q. September 16th, 1998?
A. Yeah, and this is December 7th.
Q. Correct.
A. So that doesn't fit exactly.
MS. SCHMAHL: I'll tell you what, let's take a break. And if you can put your hands on it, then I'd like to discuss Dr. Roggli's report with you just a little bit.

270

THE DEPONENT: Okay. Let me go see if I can find that.
(A recess transpired.)
(DFT. EXH. 26, Dr. Victor Roggli's Expert Report, was marked for identification.)
BY MS. SCHMAHL:
Q. Dr. Harley, before we took a break, I had asked you to check your office to see whether you could find any report from Dr. Victor Harley (sic) dated September 16th, 1998; is that correct?
A. Dr. Roggli?
Q. I'm sorry; Dr. Roggli.
A. I did not find a report with that date on it. It's possible that I wrote down the wrong date, and that the report of -- Dr. Roggli's report of December the 7th is really what we talked about, but I'm not sure. I'll continue to look after we finish this and see.
Q. I've handed you what's been marked as Exhibit 26, which is the expert report of Dr. Victor Roggli dated December 7th, 1998. Would you review the expert report, please, and tell me whether you have seen the information contained therein before today?
A. Yes, I have.
Q. Is there any information contained in

271

Dr. Roggli's report that you are relying upon in forming your opinions?
A. No.
Q. Is there any information in Dr. Roggli's report that you do not agree with?
A. There may be some minor discrepancies between his and mine, such as whether Mr. Little stopped smoking in December of '95 or in November of '95.
In general, I agree with his report.
Q. You didn't rely on anything in Dr. Roggli's report in forming your opinions?
A. No, although it's always nice to be in good company.
Q. How much time did you spend reviewing the pathology materials that you received?
A. You know, I'm not sure, it's been a while now, but probably around an hour.
Q. Reviewing all of the pathology materials under the microscope?
A. Right, perhaps a little longer.
Q. And does that include the time that you spent taking photomicrographs?
A. No.
Q. How much time would you have spent taking photomicrographs?

272

A. That probably would have taken around another hour.
Q. How much time did you spend preparing your expert report, which is Exhibit 6?
A. Probably in the range of an hour.
Q. So for the two and a half hours that you spent reviewing records, the hour that you spent reviewing pathology, the hour that you spent preparing your report, have you billed Plaintiffs' counsel for that time?
A. There's a bill here from September the 6th, 1999. The report was done August 16th, 1999, and this is for $500, so at $200 an hour, that would be about two and a half hours.
Q. So you billed them for some of the time, but not all of the time; is that correct?
A. Probably so.
Q. Did Plaintiffs' counsel or anyone from Plaintiffs' counsel ask you to limit in any way the time that you spent reviewing the materials or preparing the report?
A. No.
Q. Was any dollar limit set on the amount that you could bill Plaintiffs' counsel for for your services?
A. No.
Q. I'd like for you to turn, please, to the second

273

page of your expert report, which is Exhibit 6. There's a section, about midway down, called Tobacco. Do you see it there?
A. I do.
Q. And you wrote, quote, Mr. Little smoked about a pack of cigarettes a day for about 25 years, period, end quote.
Where did you obtain the information regarding Mr. Little's smoking history?
A. I think I got that from the medical records. I may have got some information from Ness, Motley law firm as well, but in general what I try to do is look to see what the various doctors who interviewed the person at various times have said. And those usually have quite a range. People come up with different numbers.
But I'm not sure exactly when I got access to Mr. Little's own deposition, which would be probably more accurate in that regard.
Q. Okay. And according to -- reading on in the tobacco section you wrote, quote, He quit at the time of his first surgery in December of 1995, period, end quote, correct?
A. Right.
Q. If my math is right then, Mr. Little started smoking, at least according to his medical records, in

274

1970; is that correct?
A. How old was he when he died?
Q. Well, if he quit smoking in 1995 and he smoked for about 25 years, that would put it to about 1970; is that correct?
A. Right. In my summary and comment, I said he started smoking in his 20s; he was 50-years old. So if he started when he was 25, that would give him 25 -- and smoked a pack a day, that would give him 25-pack years.
Q. So sometime in the 1970s?
A. Correct.
Q. Now, you also began smoking in the 1970s; is that correct?
A. Correct.
Q. In fact, you testified in 1997, in the Karbiwnyk case down in Jacksonville, Florida, and you testified there under oath; is that correct?
A. Correct.
Q. And in that deposition, you were asked about your smoking history. Let me just get my hands on the transcript.
Actually, on page 71 of your Karbiwnyk transcript -- and Karbiwnyk is K-a-r-b-i-w-n-y-k -- if you look on page 71 of the transcript --
Jerry, do you want a copy to look at?

275

MR. EVANS: Yes, please.
MS. SCHMAHL: You get my big copy to follow along.
MR. EVANS: Okay.
BY MS. SCHMAHL:
Q. -- you were asked -- the question was, was there any doubt in your mind, when you started, that cigarette smoking was associated with lung cancer and other diseases, and you answered, None whatsoever.
When did you first become aware that smoking was associated with lung cancer?
A. I'm not certain. I think most people thought that it was before I started medical school, when I was in college.
Q. When did you start medical school?
A. I started medical school in 1960. I was in college in the late-'50s. And I think most people at that time thought that cigarettes were related to lung cancer.
Both of my parents smoked, and when I started medical school in the '60s, I think the association between smoking and lung cancer was well-known.
Q. Was that something that was well-known just to medical students and medical professionals?
A. I don't think so. I think the general population of the United States knew about it; whereas, a

276

lot of people might not have believed it, I think most people did.

Q. After the Surgeon General published his report on smoking and health in 1964, was there any doubt in your mind that smoking was related to lung cancer?

A. As I remember it, I think I was of the same opinion of what most people was, that the report was stating the obvious at that point, that it was well-known at that point. And I don't think most of the people I knew paid a whole lot of attention to it. The government finally caught up with the rest of everybody else's understanding.

Q. So the 1964 report was just not saying anything that anyone didn't know; is that correct?

A. But it was a good summary of what people had been saying and thinking.

Q. And it did get a lot of press, right, front page of newspapers, on the evening news?

A. Right.

Q. On the radio?

A. (Moves head up and down.)

Q. Are you aware of when the Surgeon General first started requiring the warning labels on cigarettes? Was that before you started smoking or after you started smoking, if you remember?

277

A. You know, I'm really not sure. All of this stuff seems to be hazy in the distant past to me now.

Q. Would it be fair to say that you personally started smoking, despite knowing that it was associated with lung cancer?

A. Absolutely.

Q. Would you have any reason to believe that Mr. Little did not know that smoking was associated with lung cancer when he started smoking?

A. I think everybody in this country in the Western World knows that it is. There may still be people that don't believe it.

And I know that there are a lot of people who think they can get away with it or think that if they die when they're 40, they don't want to live that long anyway. So there are lots of odd reasons for smoking, but I think most everybody believes that lung cancer is related to cigarette smoking.

Q. And it's believed that to be the case since the late-'50s, early-'60s; is that correct?

A. There seems to be a population of people who catch up a little bit late. And so the percentages of people in the country who thought what, when, is kind of hard for me to say.

Mr. Little was an educated man, and he was

278

probably aware of the fact that there was a relationship between smoking and lung cancer. It's been a long time since I've read his deposition; he may have been asked that question. So it would be better if he could speak for himself.

Q. If I can get you to turn to page 165 of the transcript that's in front of you, let me read you another passage from your 1997 Karbiwnyk testimony.

You stated, and I quote, I tell people to quit smoking so they won't get lung cancer. And they say, Well, Doc, how long do I have to quit? I say five years is good, but after about 12 years, you're getting down close to the same as if you hadn't smoked.

MR. EVANS: I'm sorry; can you tell me what line you're reading from?

MS. SCHMAHL: Page 165. Do I have the wrong page?

MR. EVANS: Okay, I'm sorry.

BY MS. SCHMAHL:

Q. Doctor, do you still advise your patients to quit smoking so they won't get lung cancer?

A. Well, as a pathologist, most of the ones I see already have it or may not be with us anymore. But when I'm talking to live people who are smoking, I do tell them that they shouldn't smoke, not just for lung cancer, but

279

for all other reasons.

Q. If a patient quit smoking today, their risk of developing lung cancer declines significantly after five years; is that correct?

A. That's correct.

Q. After 12 years, their risk of developing cancer is nearly the same of that -- as that of a person who has never smoked; is that correct?

A. It comes down closer. It's an asymptotic thing. It never comes down to normal, and figures on that keep changing as more information comes in.

The dangers of smoking, with relationship to lung cancer, seem to be greater than I thought then. And I can't quote anything exactly now, but as I keep reading, the cellular events that lead to a cancer, many of which seem to be permanent, have been looked at more carefully, and I think that lung cancers in smokers are probably higher than I thought at the time.

But, in general, I think this curve that I'm describing, of a continued period of danger of lung cancer, that then drops off to some extent, and then continues down, never quite reaching the normal line, is an appropriate curve. I think that's more or less how it works.

Q. Okay. But getting down close to the same risk

280

level as a never smoker; is that correct? It will never -- it will always be higher, but approaching --

A. Right, in somebody not exposed to asbestos or some other very risky substance, it does come down close.

I will say, too, that since I've been working in Hollings Cancer Institute more closely than I had before, that I keep seeing cases of people who had stopped smoking quite a long time ago and who get lung cancer.

And those are individual observations that don't mean anything as far as a conclusion, but they do keep bringing up the question of how long does this go on?

And it's been a long time since I looked up the question of exactly -- in an organized fashion of exactly what the risk is, five, ten, 15, 20 years out from stopping. I need to do that again.

But it does come down. It's a good idea to quit. It's a better idea not to start.

Q. Let's see. Turning your attention back to your expert report, Exhibit 6, continuing on that second page about midway down, you have a section that's entitled Review of Slides. Do you see it?

A. Yes.

Q. According to your report, you examined slides from three pathology specimens; is that correct?

A. Correct.

281

Q. Fifteen slides from specimen SP95-20474?

A. Right.

Q. Eighteen slides from SP96-4435?

A. Yes.

Q. And 14 slides from SP96-16688.

A. Correct.

Q. Have you reviewed any of Mr. Little's pathology slides since drafting your expert report on August 16th, 1999?

A. I did; the ones that I took the photographs from, I looked at at the time that I took the photographs.

Q. When did you take those photographs?

A. I'm not sure exactly. I used to have a little piece of yellow paper with these that told me that date, but I'm not sure where that is now.

Q. Is there anything on the slides, themselves, that may tell you when they were developed, give you some idea of --

A. No.

Q. Can you estimate?

A. I might be able to find out from Jim Nicholson when I took the...

Q. Can you estimate approximately?

A. No. Really, he might have some record of when I had the prints made, but I'm really not sure when I took these.

282

Q. Well, can you estimate approximately how long after you drafted your expert report you took the photomicrographs?

A. According to my notes, sometime after January, '99. I said I've looked at the slides, made notes, need to photo and then Xerox slides and return.

And then 2-4-99, I said took some photos of tumor and one of bronchiolitis, parentheses, not great.

And then, apparently, I found two more boxes of something and thought I should -- needed to photo those, and I probably didn't. So I think the photographs we're looking at were taken on February the 4th, 1999.

Q. But your expert report is dated August 16th, 1999?

A. Right.

Q. So you actually took the photographs before?

A. Before then, apparently so.

Q. Okay. So you have -- the last time that you would have looked at the actual pathology materials would be sometime on or about August 16th, 1999, when you drafted your report; is that correct?

A. So far as I know.

Q. Now, earlier you testified that you spent about an hour reviewing the pathology slides when you were

283

preparing your report and about an hour reviewing the pathology slides in connection with making the photomicrographs; is that correct?

A. Right.

Q. I want to clarify your testimony from the first day of your deposition. I believe it was your testimony that you first looked at the pathology slides by holding them up to the light; is that correct?

A. Probably so, that's what I usually do.

Q. And when you hold slides up to the light, you're just looking at the pathology with your naked eye; is that correct?

A. Right.

Q. What conclusions are you able to draw from grofs observation of the pathology slides?

A. The main reason for doing that is to make sure that when I put it under the microscope and start magnifying things, that I don't miss something that's off in a corner somewhere. If I see a nodule or some abnormality with the naked eye, I then remember to look at that under the microscope.

Q. Okay. And there's no clinical diagnosis that you could make through grofs observation; is that correct?

A. Clinical diagnosis?

Q. A diagnosis of whether they have or don't have

284

cancer.
A. I think most pathologists can look at a slide from halfway across the room, and probably nine times out of ten say that's cancer, that's not. You get used to the patterns.
In lung pathology, the patterns in the lungs are things that you can see quite well with your naked eye. So there are a lot of things you do see, but they're -- looking through the microscope is more accurate.
Q. So as you hold the slides up to the light, you can, by looking at the patterns of the slide, figure out what areas of the slide you want to focus on when you actually look at it under the microscope; is that correct?
A. It helps, yes.
Q. So with the naked eye, you could see a pattern that may be suggestive of a tumor; is that correct?
A. Right. You might see that there's tumor in the whole left-hand side of the slide, and the right-hand side might be lung or connective tissue.
Q. And so then you would want to focus on the portion of the slide that has the tumor; is that correct?
A. Probably so.
Q. And then I believe you testified that you then look at the slides with a scanning lens. What is a scanning lens?

285

A. It's a low-power lens.
Q. Is that a 2.5X?
A. Usually.
Q. And then based on what you saw in the scanning lens, you chose the fields to look at higher power, right?
A. Correct.
Q. What made you choose which fields to look at at higher magnification?
A. A variety of things. If you were looking – if you were flying over a forest in an airplane, looking down, and you see all the trees and you see some clearings and you see a big tree and you see a pond and so forth, there might be something there that you wanted to look at more closely. And you -- for instance, if you're looking for ducks, you might want to go look at the pond, so you might circle down and get closer.
And the same thing is true in looking through this microscope. You might see an unusually large cell or you might see invasion of the blood vessel or invasion of the pleura, or something like that, some pattern that's a little bit different, and then to look at it more closely, use a higher power, and perhaps then use an even higher power.
Q. Okay. So you would, generally, look at the entire slide with the scanning lens; is that correct --

286

A. Right.
Q. -- the low-power lens?
And then after you scanned it, if there was something that you found unusual or interesting, then you would look at that field with the high power; is that correct?
A. Right.
Q. Now, would a scanning lens with a 2.5X, would that be a high enough power for you to be able to make a diagnosis of either small cell or non-small cell?
A. Usually. But almost nobody would do it; nobody would stop there. Almost everybody would go to a much higher power and look at the details of the nuclei and so forth.
Q. Would they go to a 20X or a 40X, or what power would you use?
A. It would be a step-wise thing, from the lowest power to a medium power to a high power. And a 40X is the standard high dry. So most people would look at tumor cells under a 40X for awhile, and then back off to the 2.5X.
Q. With a 2X scanning lens, could you distinguish cell type?
A. Usually. Understand that in addition to the objective lens, and as I sit here I'm looking at a

287

microscope there behind you, and you'll see the lenses sticking down to the bottom on the nosepiece; those are the objectives. And there are also oculars, which are the lenses on top where the eyeballs go. The oculars are usually a 10X, also.
So you multiply the two. The one on the bottom, if it's a 2.5X, it's multiplied by 10, so it's really 25X. And the cells that we're looking at are sufficiently big, that the outlines of the cells are quite clear at that magnification, but they're small and they're distant.
The difference between a small cell carcinoma and large cell is usually obvious at that point.
Q. Right.
A. Then, in looking around in the large cell tumors for evidence of differentiation that will tell you whether it's an adenocarcinoma, squamous, or not, those things are usually found also with the scanning lens, and then they're usually looked at with higher power.
Q. Okay. So the 2.5X would be enough for you to determine the classification of non-small cell cancer?
A. I would almost never stop there, but the initial impression is gained there, and it's usually pretty accurate.
Q. So I believe that you testified -- actually, when we were going through these photomicrographs that you

288

took of Mr. Little's pathology -- that at the low power lens, it was not magnified significantly for you to be able to make a classification of cell type; is that correct?

A. Meaning that in any particular case, you would use whatever tools were at hand. Bear in mind, that when a pathologist is looking through a microscope, it's a very active thing; he's wiggling things back and forth, and usually the nosepiece objectives are being flashed back and forth pretty quickly, there's a lot of stuff going on, and it's not at all like looking at a photograph.

Q. So with a 2.5, there would be features that would be suggestive of cell type to you; is that correct?

A. Right.

Q. But you, as a pathologist, would not feel comfortable making a diagnosis without looking at the field under a higher magnification; is that fair to say?

A. Right. I would feel even more uncomfortable if I had to look at one under high and couldn't use the lower power. 2.5X is the most important lens.

Q. Now, turning back to your expert report, which is Exhibit 6, the slides that are designated 95-20474, correspond to a surgical pathology report dated December 18, 1995, which has already been marked as Exhibit 17 to your deposition. Is that correct, Dr. Harley?

289

A. This solves the problem of the Victor Roggli report; in that, the date that I noted, 9-16-98, is the date of the Ness, Motley letter written to Dr. Roggli, and that's the date that I inserted here.

So apparently, this was sent to him on September the 16th, 1998, and he reviewed it at some time after that.

And then, what was your question?

Q. My question to you is --

(DFT. EXH. 27, Surgical Pathology Report dated 12/18/95, was marked for identification.)

BY MS. SCHMAHL:

Q. I'm handing you what has been marked as Exhibit 27 to your deposition. For identification, Exhibit 27 is a surgical pathology report dated December 18th, 1995.

Is it correct that the 15 slides that you received correspond to this surgical pathology report, which is now Exhibit 27?

A. Correct.

Q. Okay. So the slides designated as SP95-20474 contain biopsy material from Mr. Little's left upper lobe and anterior mediastinal node; is that correct?

A. Right.

Q. And the pathology material was collected on

290

December 18th, 1995 during an exploratory thoracotomy, correct?

A. Correct.

Q. Did you keep any notes concerning your examination of the slides from December 18th, 1995?

A. No. All I have is the single sentence here in my report, which says that sections reveal a large cell carcinoma of lung with metastasis to an anterior mediastinal node. And this corresponds more or less with the MUSC pathology report by Drs. Larisey and Wilson, which says, "Lung, clinically left upper lobe lesion, biopsy; poorly-differentiated carcinoma, non-small cell type; frozen section diagnosis confirmed," and under that, "fibroadipose and fibroconnective tissue, clinically anterior mediastinal node, excision; poorly-differentiated squamous cell carcinoma; frozen section diagnosis confirmed."

Q. Well, you say that it corresponds more or less, except that you saw large cell lung carcinoma, where they saw a poorly-differentiated carcinoma; is that correct?

A. In looking at the lung, they called it poorly-differentiated and didn't further describe it, just said it was non-small cell.

And when they looked at the mediastinal tissue, which was said to be a node, but they didn't actually see

291

a lymph node in that particular slide, apparently. They saw, again, large cell carcinoma, and they must have thought they were squamous features since they mention that.

Q. Except that they actually diagnosed it as a squamous; is that correct?

A. They call it poorly-differentiated squamous cell carcinoma. I must not have seen features which convince me that I would call it a squamous. I'm pickier than some people are about those.

Q. So the sum total of your notes, regarding your review of the December 1995 pathology, is the sentence on page 2 of your expert report; is that correct?

A. I think so.

Q. Did you take any photomicrographs of the December 1995 pathology?

A. I don't believe so. I wish I had. It would be nice to go back and look at those slides again, but I don't believe I took any photographs of them. And I think the reason was that I didn't have those slides at the time that I took the photographs, for some reason.

Q. According to Exhibit 6, your review of the December 1995 pathology showed large cell carcinoma; is that correct?

A. Right.

292

Q. Could -- and your opinion is not broken down in any way on a slide-by-slide review; is that correct?
A. Right.
Q. Can you, sitting here today, testify that all of the 15 slides that you reviewed that were designated SP95-20474 were positive for large cell carcinoma?
A. Usually, when I look at slides like this, I usually have a report like this one from Drs. Larisey and Wilson; and oftentimes, I'll scribble things on the back of it. If I did anything like that in this case, I can't find my notes right now, and I've looked, just recently in looking for the Dr. Roggli report, and I don't see that.
Q. Because we had actually subpoenaed all the notes that you had taken, all of the records that you had reviewed; is that correct?
A. Right. And you don't have them, do you? I don't seem to be able to find anything like that, either. But oftentimes I will do that, and I can't say in this case that I did or did not.
Q. But to the extent you did that, you can't find those notes today?
A. Correct.
Q. Aren't aware?
A. Right. And there were, apparently, 15 slides there, and -- which is quite a number of slides.

293

Q. Do you know whether the 15 slides were the original slides that Mr. Little's pathologist examined or were these re-cuts?
A. I don't know.
Q. Can you briefly explain what a re-cut is?
A. Yes. When tissue is removed, the process is looked at by a pathologist, it is embedded in paraffin wax so that very thin sections can be cut. The wax supports the tissue.

The very thin sections are cut, the paraffin is removed, and the tissue is then stained with dye so that it can be seen more clearly. And that tissue is mounted on a 1-by-3 inch glass slide, the histopathologic slides that we have been referring to.

The tissue, meanwhile, remains in the paraffin block so that if one wants to go back and look at more of it or do further things to it, additional sections can be cut from the paraffin block. So the tissue remains in the block, and a great many slides can be cut from the average block.

Q. Is there anything in Exhibit 27, which is the surgical pathology report, that would indicate to you how many original slides were made of Mr. Little's December '95 pathology?
A. There is not. However, records of that will be present in the computer; we could look and see.
Q. Sitting here today, could you tell me which of these 15 slides were positive for cancer?
A. No. At least one from the lung was, and at least one from the mediastinum was, and I have the impression that more than one was, perhaps all of them were, but I really can't say without looking.
Q. And you couldn't identify, today, which specific slides would have shown what you believe to be large cell carcinoma; is that correct?
A. Not without further original notes, which I don't seem to be able to find, or without the slides, themselves.
Q. Or what sort of alveoli might be present in the lungs or what sort of changes to the alveoli?
A. Right.
Q. Or whether there is a section of pleura or uninvolved lung in the samples either; is that correct?
A. Without notes, photographs, or slides, I really couldn't say.
Q. Now, can you, sitting here today, tell me what morphological features, from your review of the December 1995 pathology, were consistent with large cell carcinoma?
A. First of all, I think everybody seems to be agreeing that it's not small cell. Therefore, it must

294

295

necessarily be one of the large cell types, squamous, adeno, or without those features, simply large cell.
Q. Would you agree that the term poorly-differentiated non-small cell cancer and large cell carcinoma can be used interchangeably?
A. Yes, in general. There are unsaid, unspoken things here; in that, if features of adenocarcinoma were seen, they would have been mentioned.

If features of squamous cell carcinoma were seen, they would be mentioned, and apparently there was something in this that made somebody think it might be squamous. But absent those, the two terms are more or less synonymous.
Q. So for your purposes, if there are not enough features that you feel confident making a squamous diagnosis, there are not enough features that you feel confident to make an adeno diagnosis, then you would make a large cell diagnosis, is that correct, if you're confident that it's not a small cell --
A. If there's a fair amount of tissue. If there's a very small amount of tissue, or if I see things that make me think that if I simply had more tissue, I could say that it was adeno or squamous, then I would call it non-small cell, without committing myself to calling it large cell.

296

But if I've got a fair amount of tissue and I don't see evidence of any other differentiation, then I'd call it large cell.

Q. Okay. Do you use the term large cell and poorly-differentiated non-small cell carcinoma interchangeably?

A. No, no, I don't. And if I said non-small cell, what I'm saying is that I haven't got enough tissue to classify it further; whereas, if I call it large cell, I'm saying there is enough tissue here for me to reasonably exclude adeno or squamous.

Q. So, again, what morphological features in your review of the December '95 pathology were consistent with large cell cancer?

A. I would have seen fairly large cells. I would have seen fairly large nuclei. I probably --

Q. I'm sorry to interrupt you, Doctor. Now, are you telling me what you remember seeing, or are you basing it on the fact that you called it a large cell today, stating that this is what you must have seen?

A. I'm basing this on the fact that I made that diagnosis; this is what I must have seen. I cannot remember what I actually saw.

Q. Sitting here today, can you remember what you actually saw in December 1995 that would have been

297

consistent with an adenocarcinoma?

A. The size of the cells would probably have been consistent with adenocarcinoma.

Q. Do you actually remember that, or is this based on your general understanding and knowledge of large cell cancers?

A. I can't remember what the cells look like exactly, but that had to have been true; otherwise, I wouldn't have called it large cells. The cells have to be large.

Q. Do you have any specific recollection of morphological features that would be consistent with an adenocarcinoma?

A. Simply the size of the cells, because adenocarcinomas have large cells.

Q. Do you have any specific recollection of seeing features that were consistent with an adenocarcinoma, or again, are we going back to -- you called it a large cell, therefore --

A. Therefore, it's large cell.

Q. Right. Therefore, these are the features that you must have seen?

A. No, I cannot remember exactly what these slides looked like.

Q. Okay. And would that be fair for any

298

histological feature that I ask you about?

A. Yes. I wish I had reviewed this particular material right before I came in here so I would be able to say exactly.

MS. SCHMAHL: Would now be a good time to take a break for lunch? I know it's pushing noon, and we're kind of at a fairly decent stopping point if it's good for y'all.

THE DEPONENT: It depends entirely on you.

MS. SCHMAHL: Let's take a break, since we're at a good stopping place, and we can all grab some lunch, and I need more water.

(A luncheon recess transpired.)

BY MS. SCHMAHL:

Q. Dr. Harley, if I can review -- strike that.

Dr. Harley, if I can direct your attention to Exhibit 2 of your deposition, the back of the last page.

A. Right.

Q. Can you describe what it is that we're looking at, please?

A. These are handwritten notes made by me on first reviewing the slides in this case. This appears to be the original, and has notations at the top indicating surgical pathology numbers, a medical record number, the name Samuel Martin Little, with Martin underlined, some dates

299

of treatment of various types, his birthday, his doctor's name, a notation regarding smoking in the upper right-hand corner, a star by the statement, Two nodes with microscopic remnants at level 5.

Q. Do you know which pathology specimen number that notation corresponds with?

A. No.

A note regarding his thoracoscopy, 9-96.

Q. Then continuing down, a note concerning a CT scan of October 28th; is that correct?

A. Right.

Q. The next line says Mark Green talked with Dr. Skarin at Dana Farber Institute regarding a resulting (sic) and consultation. And then under that, 11-96, went to Boston; Skarin not ready until February '97; plan, taxol.

1-23, what's that notation?

A. Nodules, dash, striking shrinkage.

Q. Does that have to do with his response to chemotherapy?

A. Right, or radiation.

And then 4-17, it says, Nodules gone, but left mid-lung, 3 millimeter nodule present.

Q. Okay.

A. 7-97, okay. 7-31-97, letter Rasmussen to use

300

marimastat. 11-10, I think it says under that, and of whatever I was looking at, still okay.
Q. Okay. Directing your attention to the left -- I'm sorry, directing to your attention to the right lower corner, there are what appear to be pathology specimen numbers with some notes to the side of that; is that correct?
A. Right.
Q. Can you tell me, please, what you wrote for SP95-20474?
A. It says, "Node with met, large cell," then it says, "CEA, cut away, but negative."
Q. Okay.
A. That suggests to me that when the -- that the specimen was small when it went back and cut slides were getting out of the region of tumor, but there was still a little bit left, and that what was there was negative on CEA stain.
Q. Is that -- CEA is carcinoembryonic --
A. Adagen, correct.
Q. Okay. Continuing down to the SP96-4435, what is written next to that specimen number?
A. That says, "Extensive radiation necrosis of tumor, little viable tumor," question mark, exclamation point. I must have been really excited about this,

301

"radiation change, tumor cells, radiation change, too," and then out to the right it says, "radiation change difficult to evaluate," something like that. Let me see if I can see that with my glasses off, "smoker's changes" or "smoking changes."
Q. Continuing down to what you wrote beside SP96-16688, what are your notes on that?
A. Metastatic undifferentiated large cell carcinoma, CEA negative.
Q. And then continuing down the -- is this another specimen number, 98-E-876?
A. It is. And next to it, it says, "Mass Gen," for Massachusetts General, "rib," dash, "normal bone marrow not," something, "not related."
Apparently, the slides must have been sent somewhere to somebody that had a slide from somebody at Mass General. And when the slides were sent to me, that got stuck in here, so I don't think that has anything to do with Martin Little. That was somebody else's bone, rib.
Q. So that was somebody else's slide in that set, as far as you know?
A. Right.
Q. To your knowledge, are the notes that are on the back of the last page of Exhibit 2 the only notes that you

302

made?
A. So far as I remember. I didn't really remember this distinctly, but as I said, usually when I sit down at the microscope and look at slides, I use the back of a surgical path report and write notes. Oftentimes, they're more detailed than this, but this is probably all I did in this case.
Q. And there is nothing on the back of this page that would be a slide-by-slide analysis of each of these pathology specimens?
A. Oftentimes I do that, but apparently in this case, I did not.
Q. Did you have an opportunity, during the break for lunch, to go through your records or to look through your materials to see if you did have any additional notes?
A. No, I did not. The fact that this is the original strikes me as interesting, I don't usually do that, but I may have made notes right on something that was sent to me.
The other thing that I wanted to look for was the mysterious Dr. Roggli report, and I think we settled that, the fact that I just wrote down the wrong date.
(DFT. EXH. 28, Surgical Pathology Report dated 3/12/96, was marked for

303

identification.)
BY MS. SCHMAHL:
Q. Dr. Harley, let me hand you what has been marked as Exhibit 28 to your deposition. For identification, Exhibit 28 is a surgical pathology report dated March 12th, 1996, based on pathology materials collected on March 11th, 1996. And this pathology report carries the extension number SP96-04435; is that correct?
A. Yes.
Q. Turning your attention to -- back to Exhibit 6, which is your expert report, the second page, where you're discussing your review of slides. The slides designated SP96-4425 correspond to the surgical pathology report, Exhibit 28, correct?
A. Correct.
Q. Do you know whether the 18 slides you received were all the slides available from March of 1996?
A. I can't really tell, with certainty, from looking at this report. I think they were. We can, as I've mentioned, look back in the computer at the lab results and see how many were cut, but I really don't know from looking at this.
Q. Okay. Do you remember or can you tell by looking at Exhibit 28, whether you reviewed the original set of slides that Mr. Little's treating pathologist

304

reviewed, or did it include re-cuts?
A. I don't know from looking at this.
Q. The slides designated as SP96-4435 contain biopsy material from Mr. Little's left lung and its lateral lymph nodes; is that correct?
A. Right.
Q. Did you take any photomicrographs of the pathology slides from March of 1996?
A. I don't think so. Wait a minute. This is the one I took, isn't it?
No, these are all the photomics I took, and I think they are all labeled 16688; are they not?
Q. Yes, to the best of my knowledge.
A. Okay. That's all I took, then.
Q. So the answer would be no --
A. The answer is no.
Q. -- as far as photomicrographs.
A. Right.
Q. Let me just clear up what I believe is probably just a typo. On the first page of your expert report, you designate the slides at SP96-4435, which corresponds to the pathology report in front of you, which is Exhibit 28.
A. Right.
Q. And on the second page, where it says 96-4425, talking about the same slides --

305

A. It should be 35.
Q. Sitting here today, could you, if I asked, describe the histological features of each of the slides that you reviewed?
A. No.
Q. Could you describe which slides contained large cell morphological features?
A. I don't think I saw any other types of features, so anything with cancer in it would have that pattern.
Q. But could you specifically identify -- you're not contending that all of the path samples had active tumor in it, are you?
A. No, but I did not disagree with the surgical path report. So in any of those slides where cancer was found, I thought it was large cell.
Q. Could you, today, tell which of the slides that you looked at had features that would be consistent with an adenocarcinoma?
A. I can only speak generally, in that there are certain features that large cells and adenos share which would have been present in all of these with the cancers, but there must not have been any significant adenocarcinoma pattern, because I didn't remark on it.
Q. And you're aware from the notes that you made on the last page of Exhibit 2, that this pathology material

306

was collected after Mr. Little had begun radiation and chemotherapy, correct?
A. Correct.
Q. And I believe that you noted in your review of the March '96 pathology materials that there was significant necrosis; is that correct?
A. Yes.
Q. Would you agree with Dr. Thomas Carico; is that correct --
A. Carico.
Q. -- Carico, and Dr. Timothy Smith, that nearly all of the tumor is necrotic?
Do you see that on Exhibit 28, on the last page, under diagnosis, there is a comment that says, quote, nearly all of the tumor is necrotic, only microscopic remnants are present?
A. My memory of this is that there was a great deal of necrosis, but that there was a fair amount of viable cancer left. A lot of it changed by the radiation. I remember this because it was an interesting-looking change, unusual looking.
But in general, there was a great deal of necrosis, whether one would say nearly all or not would depend on what one's concept of "nearly all" is.
Q. So you would agree that there was a great deal

307

of necrosis, but maybe wouldn't go so far to say that nearly all of the cancer was necrotic, is that correct?
A. Right.
Q. Is there anything inconsistent with the findings of the diagnosing pathologist in March of 1996, where he diagnosed the cancer as being poorly-differentiated carcinoma and your finding that it was large cell carcinoma?
A. I wouldn't disagree with their calling this poorly-differentiated carcinoma. I had the advantage of looking at all of the material at once. And they may very well have done the same thing, too. In fact, they probably did, since it was called squamous at one point prior to this.
But I wouldn't disagree with they're calling it poorly-differentiated carcinoma, large cell, not small cell.
Q. But my question was, is there anything inconsistent with their diagnosis of poorly-differentiated carcinoma and your diagnosis of large cell?
A. No. I think we're talking about the same thing, and that, part of the reason I called it large cell is for the sake of consistency, that that's what it had been, and even though it was changed by radiation, I didn't think it was a different tumor that occurred.

308

Q. So because you saw what you believe to be large cell in the 1995 pathology materials, when you were examining the slides taken from the March of 1996 pathology, that helped support your opinion that it was a large cell; is that correct?
A. Right. I thought it was the same tumor.
Q. Do you have any recollection as to whether, just looking at the March of 1996 pathology, you would have diagnosed it or could have diagnosed it as a large cell carcinoma?
A. I think I could have said that it was not small cell.
Q. Okay.
A. And beyond that, considering the degree of necrosis and damage that was there, I think I probably would have had difficulty further classifying it.
Q. Now, I just want to clarify with you some of the effects of radiation and chemotherapy on both cancer cells and lung tissue, in general.
Would you agree that radiation and chemotherapy result in necrotic cells?
A. Yes.
Q. Would you agree that necrotic cancer cells have a different appearance than viable active cancer cells?
A. Right, I do.

309

Q. Is it possible to determine cell type under a microscope by looking solely at necrotic cells?
A. No, although one can often say that it's not small cell, because the cytoplasm is oftentimes still visible, just not well preserved.
Q. But as far as classifying the subcategories of non-small cell cancer, would that be possible with necrotic --
A. Sometimes, usually not. If there's a nice keratin pearl, a lot of times that can still be seen, and you can say, a-ha, squamous.
If there are glands, even though they're dead, they may still look like glands, and you say a-ha, adenocarcinoma. But oftentimes, after radiation, chemotherapy or tumor necrosis just de novo --
COURT REPORTER: Or what? I'm sorry.
THE DEPONENT: D-e, n-o-v-o -- one cannot categorize the tumors.
BY MS. SCHMAHL:
Q. Do you see cancer cells that are at the periphery of an area of necrotic tissue; would they look different?
A. If the necrosis were caused by radiation and perhaps by chemotherapy, but certainly radiation, they frequently do look different, not always, but usually they do.

310

Q. And what we're talking about is the live cancer cells?
A. Right.
Q. So if you have an area of necrosis, and then you have an area of viable tumor, the viable tumors that abut the necrotic cells will often look different; is that correct?
A. Yes.
Q. Would they often look atypical?
A. Well, atypicality is a term that is usually applied to benign cells that have some changes resembling cancer.
So when it's used in describing a cancer cell, it's usually used in a sense of saying unusually atypical or remarkably atypical or something like that, because it's sort of a given that cancer cells are atypical.
Q. If you had adeno cells that were live and they were abutting a large area of necrotic cells, would they look different than the typical adenocarcinoma cells?
A. They could. They frequently do.
Q. Directing your attention back to the review of slides on Exhibit 6, page 2, continuing on with your analysis of the March 1996 pathology, you state that radiation changes are noted in the lung away from the tumor as well.
Do you mean radiation changes in the left lung, in the left uninvolved lung, or in the right lung?
A. Exactly -- oh, this is under 4425?
Q. Yes.
A. This is radiation change in the lung adjacent to the tumor seen under the microscope.
Q. So this would be the left lung, but in the area of the lung that was not -- that did not have tumor involvement?
A. That did not have tumor in it, correct.
Q. Other than necrotic cancer cells, fibrosis, and cancer cells that had an unusual morphological feature, did you see any other radiation changes?
A. Well, yes, there was a lot of radiation change in the previously normal tissue which had been damaged by the radiation, resulting in fibrosis and cellular atypia and leakage of nuclear proteins out of the nuclei and that sort of thing.
Q. Let's continue down in your expert report to your review of SP96-16688.
Let me hand you what was marked in your previous deposition as Exhibit 22. The pathology slides that you reviewed correspond to Exhibit 22; is that correct?
A. Yes.

311

312

Q. Those that are designated SP96-16688, right?
A. Correct.
Q. And that was the pathology report created on September 18th, 1996?
A. Yes.
Q. Okay. In the fifth sentence on page 2 of your report, and I'm referring back to Exhibit 6, you wrote, quote, numerous small nodules appeared in both lungs and one of these was removed by thorascopy. This material is represented by the 14 slides labeled SP96-16688, correct?
A. Correct, yes.
Q. Okay. Is it your understanding that the 14 slides you received for the September 1996 pathology all came from a single nodule?
A. I think that was my understanding. It occurred to me that I usually Xerox copies of the slides, and I may have done that in this case, and I may have sent Ness, Motley back a copy of that, and you may have a copy of it.

The Xerox copies of the slides, which include the labels, would say whether they were re-cuts or not and what special stains were there and that sort of thing.

The report here, now, coming back to this particular specimen, says, "received fresh, for intraoperative examination, is an approximately 4 centimeter lobe of lung. A representative section is

313

frozen. The remainder of the tissue is set aside in A-2."
Q. Was it correct that there were actually, looking under the tissue source on Exhibit 22, at the top, that there were actually two nodes that were taken?
A. It looks as though there were two biopsies taken. There's A from the right lower lobe, and B, also from the right lower lobe.
Q. Okay. And sitting here today --
A. And A is a -- there's a typo in the diagnosis in which they say biopsy of left lower lobe, and then below that, the second specimen, excision biopsy right lower lobe.

The tissue source, A and B, both say right lower lobe. So what was there is two biopsies from the right lower lobe.
Q. Okay. So I just want to clarify. In your expert report, where you say that you looked at pathology from one nodule, would that be correct?
A. Probably not. I probably -- and 14 slides is an awful lot of slides to come from one nodule. It's much more likely that I looked at two, that I looked at specimens from two nodules, but both from the right lower lobe.
Q. And one nodule was positive for cancer and one was negative for cancer; is that correct?

314

A. Correct.
Q. And the treating pathologist who prepared Exhibit 22 found focal fibrosis and changes suggestive of pneumonia in the tissue sample A; isn't that correct?
A. That's correct.
Q. Mr. Little's treating pathologist also diagnosed tissue sample B as a poorly-differentiated carcinoma; is that correct?
A. Correct, yes.
Q. Is there anything inconsistent with your findings of large cell carcinoma in this tissue sample taken from September of 1996, and the diagnosis made by the treating pathologist?
A. No. I think large cell is slightly more specific than poorly-differentiated in that poorly-differentiated could be a small cell or a large cell, and it's important that it not be thought to be small cell.

So I think this is just simply, again, keeping the diagnosis consistent and saying that we think this is the same cancer, using the same term that was used in the previous report.
Q. And under which, biopsy of sample B which was positive for cancer was very small; is that correct?
A. Correct.

315

Q. They note that it was less than a half a centimeter in diameter; is that correct?
A. It says approximately 0.5 centimeters, yes. And then in the diagnosis, it says maximum dimension, 0.5 centimeters.
Q. So that's at the biggest point?
A. Pretty much a half a centimeter tumor.
Q. Which is, for us non-metric types, about a quarter of an inch; is that correct?
A. Right.
Q. If you had examined the slides taken in September of 1996, without the benefit of having examined the December 1995 and the March of 1996 pathology slides, could you have made a diagnosis of large cell?
A. I think I would have. I think the photographs that I took were from this one, because it seemed to have the clearer histology; it hadn't been affected by radiation directly.
Q. So even with --
A. I definitely would have said it was not small cell. And in the absence of features of adenocarcinoma or squamous cell carcinoma, I probably would have said it's large cell carcinoma.
Q. But you did find, at least, some features that were consistent with adenocarcinoma; is that correct? You

316

did find at least one slide where there was active tumor involvement where it appeared that the cancer was trying to create a gland.
A. Correct.
Q. Is it correct that with a very, very small biopsy sample, that it is more difficult to be able to differentiate between a large cell and perhaps what would ultimately be an adenocarcinoma or a squamous cell?
A. The smaller the sample, the more difficult to subcategorize, yes.
Q. Have we discussed fully the photomicrographs that you took from this September of 1996 pathology material?
A. I should say so.
Q. Okay. Have we fully discussed your review of the September of 1996 pathology materials?
A. Yes.
Q. Going back to your expert report, starting at the bottom of page 2 --
(The proceedings were interrupted.)
BY MS. SCHMAHL:
Q. Do you need to get that?
A. Just a moment.
Could we stop for just a second?
Q. Sure.

317

(Off the record.)
MS. SCHMAHL: Madonna, can you read where we were when we left off?
(The Court Reporter read the question commencing on page 316, line 15 and concluding on page 316, line 19.)
BY MS. SCHMAHL:
Q. Returning to your expert report, which is Exhibit 6, towards the bottom of the second page, you start a section called Summary and Comment. Do you see it there?
A. Yes.
Q. Looking at the second sentence of that section, you state, quote, The cancer responds to chemotherapy and radiation, comma, and the main tumor mass was removed, comma, but the tumor behaved in typical fashion and recurred, end quote.
The cancer spread to involve both lungs; is that correct?
A. Yes.
Q. Now, when you testified in 1997 in the Karbiwnyk trial, you testified that you were not generally involved in prescribing chemotherapy and radiation treatments; is that correct?
A. That's true.

318

Q. Is that still the case today?
A. Yes.
Q. It would be Mr. Little's oncologist who would be responsible for establishing the course of treatment; is that correct?
A. Correct.
Q. Do you agree that Mr. Little's treating oncologists are in the best position to assess the clinical course of his treatment?
A. Yes.
Q. And in this case, Mr. Turrisi, Dr. Turrisi was Mr. Little's radiation oncologist; is that correct?
A. That's correct.
Q. In fact, Dr. Turrisi is the head of the radiation, oncology department; is that correct?
A. He is.
Q. Let me read you a passage from Dr. Turrisi's testimony that was given in this case on January 7, and ask whether you agree or disagree.
And for the record, I'm reading from page 50 of Dr. Turrisi's transcript.
Dr. Turrisi -- I'll give this to you to look at.
(Tendered document.)
BY MS. SCHMAHL:
Q. There at the top of page 50, states that, quote,

319

Mr. Little's lung cancer is not the garden variety of squamous cancer. It did behave differently in my experience and in most people's experience. I've talked about him to people around the world a number of times about how he responded to the chemotherapy and how well he responded and how well he lived.
Do you agree with Dr. Turrisi's opinion that Mr. Little's response to treatment and quality of life were not typical of a squamous cancer?
A. Well, I'm certainly not going to disagree with Dr. Turrisi about clinical response of lung cancer to radiation therapy. And so I do agree with him.
And I think that in my summary, when I say the cancer responded and the tumor behaved in typical fashion and recurred, all I meant is that most people who get treated for lung cancer eventually suffer recurrence, that the tumor usually comes back and usually kills them, in fact, nearly always.
And that's the -- that's what I meant by the word "typical."
Q. So you are --
A. Now, there are other features of Mr. Little's case which are not the usual response.
Q. So in that statement and your summary and comment about the cancer's response, you weren't meaning

320

to express an opinion on his clinical course; is that correct?
A. Right. All I -- well, yes, in that it's been my experience that after people are treated for lung cancer with chemotherapy and radiation, that the cancer almost always comes back, recurs, and kills them. That's just what it does. And that's all I meant by that.
I didn't mean that his response was not unusual or that the pattern of spread was not unusual. And Dr. Turrisi was talking about the typical squamous cell cancer, and this certainly is not like that.
Q. Okay. If I could get you to turn to the next page, which is page 51 of Dr. Turrisi's January 7th deposition.
A. Okay. Next page?
Q. Uh-huh. Dr. Turrisi also testified, quote, I agree with what you said about this, that his pattern spread the way he behaved. If you had asked me to describe this for you, I'd say it's like a BAC.
Would you agree that Mr. Little's cancer actually spread like a BAC?
A. In that he had multiple intrapulmonary metastases, that is one of the things that BAC does, yes.
Q. Do you --
A. However, the diagnosis of BAC is -- needs to be

321

made by the pathologist. It has to look like one.
Q. Right now, I'm just talking about clinical course.
A. Right.
Q. Clinical course, do you have any reason to disagree that the metastatic spread of Mr. Little's disease was most consistent with a BAC?
A. No, this is very much like what a BAC can do.
Q. Okay. If you turn your attention to page 54, which is, again, Dr. Turrisi's January 7th deposition, Dr. Turrisi testified that Mr. Little's clinical course was more typical of a BAC than an adeno, and more typical of an adeno than a squamous cell cancer.
Do you see that reference?
A. Right.
Q. Do you agree with Dr. Turrisi's opinion that, clinically, Mr. Little's BAC -- I'm sorry, strike that.
Would you agree with Dr. Turrisi, that the clinical course of Mr. Little's cancer was more consistent with a BAC than any other form of cancer?
A. The pattern of spread multiple lung nodules is more like a BAC, certainly, than a squamous cell. Of course, BAC is an adenocarcinoma, and the usual solid adenocarcinoma oftentimes will go -- will spread through the lung that it starts in, go to the pleura and go to

322

other organs to a greater degree than happened in this case before it spreads to the other lung.
So this pattern is not, from the standpoint of radiology, and where the tumor went first, is not inconsistent with a BAC.
Q. Okay.
A. I mean, it's -- it's -- I wouldn't say characteristic, but it's fairly typical of BAC. Again, Dr. Turrisi has more experience with radiologic patterns than I do.
Q. Okay. My question is, do you have any reason to disagree with Dr. Turrisi's opinion that Mr. Little's clinical course was more consistent with a BAC than any other form of cancer?
A. I guess if he says so, it must be right.
My experience with BACs is that they do not respond very well to radiation or chemotherapy. I think that this tumor responded better to radiation and chemotherapy than the usual BAC. BAC is usually a very well-differentiated tumor. The tumor cells are more nearly like normal cells.
In order to get a good response from the tumor, the tumor needs to be different from the normal tissue. Otherwise, you end up with necrosis of a lot of normal tissue.

323

The nice thing about radiation, unlike chemotherapy is it can be directed a lot more specifically. So -- and this is a very good radiation oncology department. They're very good at getting the radiation in from a lot of different angles so that it concentrates into the tumor.
And I don't know whether this remarkable response was because of their expertise mostly, or because of -- some innate peculiarity of the tumor, exactly what.
But in most cases, a BAC that I've seen, the response to chemotherapy has been not very good, and the response to radiation has been not very good, because the tumor's, almost by definition, well-differentiated. So in that respect, I think this is unusual.
Now, Dr. Turrisi knows a lot more about this than I do, and the oncologists do, too. I think this is a little -- this would be unusual behavior for a BAC to my way of thinking.
Q. Are you -- have you had a great deal of experience with the protocol that Mr. Little was undergoing?
A. No, have not.
Q. Do you have any information or idea on what the response of different cell types has been to that particular protocol?

324

A. I think it's been working fairly well. That's been my impression, from listening to people talk. And I know that Mr. Little was disappointed that he couldn't be included in the therapy in Boston that he went there for, but as I remember it, he responded quite well when he came back to the protocol that he was put on.
Q. Okay.
A. So obviously in his case, it seemed to work fairly well.
Q. Would it be fair to say that, at least with respect to Mr. Little's clinical course and what cell type it was most consistent with, you would defer to Mr. Little's oncologist?
A. Absolutely, positively.
Q. Returning back to your expert report, Exhibit 6, in the summary and comment section at the bottom of page 2, actually at the very bottom of page 2, you write that cigarette smoking causes most lung cancers, correct?
A. Correct.
Q. And that this is common knowledge and accepted throughout the medical/scientific community?
Is it fair to say that your opinion is based upon epidemiological data?
A. Yes.
Q. In the Karbiwnyk case in 1997, you testified --

325

if you'd look at page 170 of the Karbiwnyk transcript, you were asked, Would you agree that epidemiology looks at the association between agents and conditions and disease and population groups? And you responded yes. Right?
A. Right.
Q. And then you were asked, And that isn't designed to try to prove causation in an individual person's disease, and you responded, That's correct; is that right?
A. Right.
Q. Do you still agree that epidemiologic data is designed to assess statistical associations and not causation?
A. Yes, although it certainly sheds some light on causation.
Q. Certainly. Continuing, if you would, in the Karbiwnyk deposition transcript, it starts at the bottom of page 170 and then continues on to page 171. You were asked, continuing that same line of questioning, And that epidemiology is based upon statistics, and you responded yes. Correct?
A. I responded exactly -- oh, yes. I said, Yes, epidemiology is based upon statistics; I said yes, yes.
Q. And then the follow-up question was, And that statistics are not very helpful in trying to ascertain one person's illness. And you responded, Exactly.

326

A. Yes.
Q. Do you still agree that epidemiology is based upon statistics?
A. Yes.
Q. Do you still agree that statistics are not very helpful in determining the cause of a specific person's disease?
A. Gosh, I hate to disagree with myself. It's obvious that any one case can be different. Statistics are not very helpful in trying to ascertain one person's illness.
Q. And you responded, exactly. Correct?
A. I did. I think I know what I was talking about, and I still think that there's a lot of -- that there's a lot of room for argument in any one case in a statistical population. But that after the results are in, and some ideas about causation have been inferred, that they can be applied to any individual case, and you can say that it's more likely that any individual case was caused by whatever you decided was causing the general problem.
Q. And that actually is --
A. I mean, I hate to beat around the bush like that, but this is kind of hard to do.
Q. Yeah, and actually the testimony you've just given is, would you agree, exactly opposite of your

327

testimony in 1997, where when asked the same question, that they were not helpful, your response was, Exactly. And today your testimony is that, in fact, they are very helpful in determining a specific person's disease; is that correct?
A. I think they are very helpful in specific cases.
Q. What has changed --
A. Although in an individual case, there's always, you know, room for doubt. And that individual case has to be looked at to see how well it matches the rest of the cases.
Q. Okay. And what has changed between when you gave your sworn testimony in 1997 and today that would cause you to have an opposite answer? Have you reviewed any new statistical data?
A. No.
Q. Have you conducted any research?
A. No, I think I'm just thinking about it differently.
Q. And how is that? Would you explain that?
A. When the question was asked originally -- and I notice that for some reason there's an objection to the form of the question. I have no idea what the lawyers are talking about there.
But when I was asked that originally, it

328

immediately brought to mind the fact that it's hard to apply a statistical inclusion to any one -- conclusion to any one case, off the bat, without further thinking.

For instance, if one said that eight or nine out of ten people with lung cancer are cigarette smokers, and you picked an individual person out of a crowd, and you said, all of these people have lung cancer, is that person a smoker? I couldn't say with absolute certainty.

I could say, well, the statistics would say that I'll be right if I say yes, 80 or 90 percent of the time. And I'll be wrong if I say yes, 10 or 20 percent of the time.

So I think that statistics can be useful in individual cases. And I notice that before I answered with the one word "exactly," now I've amplified on it perhaps too much, but I think what I've just said reflects what I think more accurately than what I thought before.

Q. Okay. Would you agree that an animal study in which human type lung cancer was induced from whole cigarette smoke, would be a far superior means of showing causation?

A. Than statistics?

Q. Than statistics, yes.

A. If -- again, I wish I could answer that cleanly and shortly.

329

Q. Let me rephrase the question then.

A. Okay.

Q. As a scientist, would you prefer to rely on statistics or animal models?

A. I think in my experience, that I'm a little leery of both of them, but that statistics have given me more interesting insights into human disease than animal models.

There are a lot of animal models that are precise and exact and tell an answer, but there are more animal models that are slightly off the mark, that produce some disease that's not at all what one sees in people, because the animals are different, more often because the exposure is different.

So I think I trust statistics a little more than I do animal models. And in each case, I have to look at the individual question and make up my own mind about how the study was done.

Q. Okay. In this case, what epidemiological studies are you relying upon for your opinion that cigarette smoking causes most lung cancer?

A. It's been so long since I collected these, that it's hard to state, but the ones in the early Surgeon General's report come to mind and the original Doll studies, I think English-smoking doctors, started off

330

telling the story quite well.

And it then -- which ones are the best out of thousands? I'm not sure. I like the early ones.

Q. The ones that come to mind are the English-smoking doctors. The ones that are in the Surgeon General's report, are those referred to CPS-2; I believe they're something like current population studies?

A. Yeah, I would -- if you gave me the Surgeon General's report, I could probably go through and pick out the ones that I've actually read sort of carefully and believed more.

Q. Now, would you agree that many substances have a statistical association with lung cancer?

A. That, I'm sorry?

Q. Many substances have a statistical association with lung cancer?

A. Oh, yes.

Q. Would you agree that epidemiological data has shown a statistical association independent of cigarette smoke for the following: Radon?

A. Yes.

Q. Asbestos?

A. Yes.

Q. Caustic agents?

A. They can.

331

Q. Exposure to carcinogens in the workplace --

A. Yes.

Q. -- also known as occupational exposures?

A. Yes.

Q. And those would be the type of carcinogens that are tracked by OSHA, the government Occupational Safety and Health Office; is that correct?

A. Right.

Q. There have been statistical studies about a high-fat diet having a relationship to lung cancer; is that correct?

A. Right.

Q. Alcohol?

A. There have been some. There have been others, more that found no clear relationship.

Q. So some studies say yes, some studies say no?

A. Right, if the smoking question can be fully excluded from it, I don't see a relationship.

Q. How about opiates?

A. Opiates.

Q. Use of opiates?

A. There are some studies that suggest that.

Q. Genetics?

A. Absolutely.

Q. A family history of cancer?

332

A. Yes.
Q. Previous non-neoplastic lung infections?
A. Right.
Q. Let me hand you what will be marked as Exhibit 29.

(DFT. EXH. 29, 3/90 Article entitled "Pulmonary Reactions from Illicit Substance Abuse," from Clinics in Chest Medicine Journal, was marked for identification.)

BY MS. SCHMAHL:
Q. For identification, Exhibit 29 is an article entitled "Pulmonary Reactions from Illicit Substance Abuse," and it is dated March 1990; is that correct?
A. Correct.
Q. And you are one of the authors of Exhibit 29.
A. Right.
Q. Your article was published in the Journal of Clinics in Chest Medicine; is that correct?
A. Clinics in Chest Medicine, yes.
Q. Is that a peer review journal?
A. I'm not sure. I participated in this with Drs. Heffner and Schabel, and John Heffner is really the first who wrote this.
Q. Is it --

333

A. And then I sort of corrected parts of it and showed the photomicrographs that are here and wrote most of that section of it.
Q. So you did review the entire article, I take it?
A. Yes.
Q. Did you also review the end notes that are cited in the back of Exhibit 29?
A. I did, but these were -- most of these were chosen by Dr. Heffner, and I did not read all of these, these references.
Q. So you have authored an article where you are not certain whether the articles and studies that you rely upon in the article are good science; is that correct?
MR. EVANS: Object to the form.
THE DEPONENT: I would say that the ones that refer to any section in the section that I wrote, I must have believed anything I referred to.
The ones that Dr. Heffner referred to, I would assume, because I think of him of being an excellent scientist and physician, are probably well-chosen.
BY MS. SCHMAHL:
Q. Can you tell me, please, by page number, which of the sections that you actually wrote in Exhibit 29?
A. Okay. Go to page 154 -- I'm sorry, let's go to

334

153.
Q. Okay. Where does your section start?
A. I inserted various things on page 153; the photomicrographs on 154, I took; the legends having to do with the photomicrographs, I wrote.
Q. Is there any text where you have written the entire section or primarily the entire section?
A. I don't think so. I think the only things that I was -- that I wrote without much revision by Dr. Heffner, are the description of the figures, the little legends, and the remaining things that are in here that I wrote would be individual sentences and statements that I stuck in on a base that he had already written.
Q. Okay. In Exhibit 29, your article studied, among other things, the harmful affects of marijuana and cocaine on the lungs; is that correct?
A. Right.
Q. Marijuana and cocaine are both opiates, right?
A. I wouldn't exactly classify them that way, but you can use them that way, yeah, yes.
Q. If you would, please turn to the last sentence on page 158 which continues on to page 159. Your article states that, quote, Marijuana is poorly combustible, producing 50 percent more polyaromatic hydrocarbons compared with tobacco and more tar sterols and other

335

products that are irritative to airway mucosa; is that correct?
A. Right. This is giving a reference number to 105, I think.
Q. Do you still agree with that statement?
A. Yes.
Q. Okay. Then, at least according to what was published here in your article in 1990, the substances in cigarette smoke that are believed to be cancer causing, are also present in marijuana smoke, correct?
A. Some of them are, yes.
Q. The polyaromatic hydrocarbons?
A. Right.
Q. Tars?
A. There certainly are carcinogens in marijuana.
Q. And at least according to your article, they're present in considerably higher amounts, is that correct, 50 percent more?
A. Right, although the smoking patterns aren't the same.
Q. Can you please tell me what is a Valsalva (ph) maneuver that's referenced further down on page 159?
A. It refers to a matter of holding the breath, pushing -- increasing pressure into the chest alters venous return to the heart.

336

Q. Is this something that is unique to marijuana smoking and other types of illicit drugs?
A. The deep inhalation and holding the breath can change the deposition of tiny particles. I think that's what that refers to. Is that what you're getting around to?
Q. I guess what I'm asking is, is the Valsalva's maneuver something that cigarette smokers do when typically smoking?
A. No, I don't think so; I've never seen one do that.
Q. Okay. Cigarette smokers typically have a full inhalation with cigarettes? Are you aware of any published literature to that affect?
A. Well, there's a whole lot of literature on patterns to smoking, and I think I've already stated that I'm not an expert on that. I've read a modest amount of that, and I've watched people smoke, and the patterns vary all over the board.
Q. What is the affect on the Valsalva's maneuver with depositing substances in the lung?
A. The -- primarily the holding of the breath, so that small particles will have an opportunity to be moved around in the lung and -- let me see if I can state this more clearly.

337

When smoke is inhaled into the lung, the airflow that one associates with inhalation actually stops at the respiratory bronchiole, so that the particles in the smoke actually don't go very far out in the lung by the mass flow of air.
When they get to that point, the airflow more or less stops, and the molecules of oxygen then go out into parts of the lung where there are fewer molecules. Molecules of carbon dioxide do exactly opposite, move back up to the bronchioles.
And in this rush of molecules in and out, particles of smoke that are hanging there in the air jump around. They get hit, essentially, by all these moving molecules and bounced around all over the place, so that the tiny particles of smoke bounce around, actually move farther out into the lung, and if they come close to a wall of an alveolus and get bounced into it, they stick. So once they stick, they can be absorbed into the bloodstream. And if there's a chemical there, the effect of that will enter the bloodstream.
If the particle containing the chemical never encounters the wall of an alveolus or a bronchus, if it just hangs there, and then is exhaled, it obviously can't do anything. The drug that's in it is never delivered.
So in the case of cigarette smoke, you see the

338

smoke go in, then you smoke come back out. Smoke that comes back out has never hit a wall, has not entered the body, and it's only about 50 percent of the smoke that went in, the other half is still in there somewhere, but what comes out is never delivered in the form of a pharmaceutical dose.
The Valsalva maneuver, just simply holding breath, in fact, can increase the dose of any substance that is hanging there in the smoke particles. They have longer to hit a wall.
COURT REPORTER: They have what?
THE DEPONENT: Longer, more time to hit a wall.
BY MS. SCHMAHL:
Q. Turning back to page 171 of your Karbiwnyk deposition transcript --
A. Which one is it? That's Turrisi's.
Q. That's Turrisi's.
A. Karbiwnyk.
Q. On top.
A. Okay. To page, I'm sorry?
Q. 171. It would be fairly close to where we were reading from previously?
A. Right.
Q. You had testified in 1997, that statistics can

339

be frequently misleading. Do you see that question and answer?
A. Right.
Q. Do you still agree that statistics can be frequently misleading?
A. Yes, they can.
Q. Do you agree that epidemiological studies that do not control for confounding factors can be and are misleading?
A. Yes.
Q. Back to your expert report, in the section called Summary and Comments, you state in the second paragraph there, quote, There is no history of occupational exposure to asbestos, comma, uranium, comma, or other substance known to be associated with lung cancer, correct?
A. Right. I have, of course, found out more about that since then. I didn't realize that -- at the time, there was some history of having smoked marijuana, and I'm not sure of what other possible carcinogens he was exposed to, realizing that everybody's exposed to carcinogens, commonly.
I think of the ones that caused lung cancer, that cigarette smoke seems to be the main one in this case. There are other ones, actually.

340

Q. Actually, there was not a question pending at the moment, but we will certainly get back to that.
My question to you is, what is the source of -- what evidence supports your finding that Mr. Little had, quote, no history of occupational exposure?
A. I didn't have a history of occupational exposure, so I didn't know of any occupational exposure. Obviously, if I state there's no history of occupational exposure, that's to the best of my knowledge. There might be something out there that I don't know about.
Q. Are you aware of any document that actually states, in his medical records, anything anywhere, that states Mr. Little had no history of occupational exposure, or anything to that affect?
A. No, and I would hate to have to go back through all the medical records again looking for that statement. I, obviously, did not see the history of an occupational exposure there in my review of the records.
Q. Are you aware that no treater asked Mr. Little about his work history or his occupational exposures?
A. No.
Q. Would that have been the sort of information that would be relevant to your opinion as to whether he had occupational exposures or not?
A. Yes, it would.

341

Q. Other than reviewing Mr. Little's medical records, did you review any other materials for information concerning risk factors that Mr. Little may have been exposed to?
A. Unless Ness, Motley sent me something that I can't remember right now, no, and of course depositions.
Q. So if Mr. Little's medical records were silent as to work history, you assumed he had no occupational exposure; is that correct?
A. Right.
Q. And if Mr. Little's medical records were silent as to his family history of cancer, you would assume that that was not a risk factor for him?
A. I thought that there was a statement in there that someone in his family had had cancer, but I can't remember exactly.
If -- I would be surprised of the medical records to that extent, not to find some statement about family history.
Q. Because that, too, would be relevant to your opinion as to causation; is that correct?
A. Well, that, and because it's a usual thing to ask. These are good doctors, and they do usually ask those questions. They don't always write them down.
Q. Let me direct your attention to Exhibit 7, which

342

is you're your tobacco chapter from the Dail and Hammar book. If you would turn, please, to page 839 under the section entitled Epidemiology.
A. Okay.
Q. There in the right-hand column of page 839, the second paragraph, you wrote there, The carcinogenic effects of tobacco were first recognized some 200 years ago. A number of studies have shown a clear-cut dose response between lung cancer mortality and number of cigarettes smoked per day, with heavy smokers having 25 times as many lung cancers as non-smokers. The use of filters results in a small but detectable difference. Correct?
A. Right.
Q. Do you still agree with that statement?
A. So far as I know. It's been a long time since I did this.
Q. How do you define "heavy smoker," as used in your article?
A. I think of a heavy smoker as somebody who smokes more than a pack a day.
Q. Do you agree that heavy smokers have a higher incidence of lung cancer than light to moderate smokers?
A. Yes.
Q. Do you agree that people who smoke high-tar

343

cigarettes have a higher incidence of lung cancer than people who smoke low-tar cigarettes?
A. I think that's true, although there's a matter of dose of carcinogen to be considered; that is, if you smoke more low tar, you can end up with the same dose.
Q. Assuming that an individual smokes the same number of cigarettes, would you agree that individuals who smoke high-tar cigarettes will have a higher incidence of lung cancer than those who smoke low-tar cigarettes?
A. If the studies are done right, they could. So I think that there should be such a relationship. There are all sorts of factors to consider, the method of reducing the tar. It all comes back to dose again.
And also the statement about epidemiology statistics in any one individual, that's even more a factor in a question like that than it is in some of the other broader issues.
Q. Okay. But at least with respect to your understanding of the dose-response relationship, if you smoke a higher dose -- strike that.
If you smoke a high-tar cigarette, you're getting higher dose of carcinogens; is that correct?
A. That's right. If the cigarette was smoked the same way, and one has a lot of carcinogen and one has less, then the more carcinogen, the more cancer.

344

Q. Okay. And are you aware of epidemiological data that has, in fact, found that the higher tar cigarettes had a higher instance of lung cancer than lower tar cigarettes?
A. I have seen that.
Q. Do you know how much the risk of contracting lung cancer decreases for people who smoke filtered cigarettes versus unfiltered cigarettes?
A. No, I've read several studies, and they were contradictory. I used to read these when they first came out, when people were, I guess, looking to see how much affect the low-tar cigarettes were going to have. And the study started perhaps too soon, after people started using those cigarettes, considering how long it takes to get a cancer.
And the first statistics that came out that I read, and I'm not sure what they were, were not at all convincing. Later, there seemed to be more of an affect in some of the later studies that I've read.
Q. And that has to do with the latency period; is that correct?
A. I think so, and the continuing change and the manufacture of the cigarettes, too.
Q. And at least, according to your book chapter, these with filters do result in a detectable difference in

345

the incidence of lung cancer, correct?
A. I thought so.
Q. Do you know whether Mr. Little smoked filtered or unfiltered cigarettes?
A. My understanding is that he smoked filtered cigarettes and switched to very low-tar cigarettes for some time toward the end of his smoking history, but it's been a long time since I read that deposition. I can't remember the details.
Q. Doctor, you don't purport to be an epidemiologist, do you?
A. Absolutely not.
Q. Could you then testify as to what Mr. Little's relative risk of developing lung cancer from his exposure to Radon would be?
A. I didn't know he had an exposure to Radon. I mean, there's a little Radon around all over the place, but I'm not -- I didn't know that he had a known exposure. I didn't --
Q. I'm asking you, can you tell me what his relative risk of developing lung cancer from Radon would be, whether it was no increased risk, or you don't have enough information, or whether there would be an increased risk?
A. Well, I'm not an epidemiologist. I am a doctor

346

that looks at cancers in lungs a lot.
If you gave me convincing evidence that he was exposed to a lot of Radon and the time period and latency fit, then I would end up saying that it's possible that Radon had something to do with it; if it were a high dose, I might say probable. But I guess the right answer is no, I don't have enough information in this case.
Q. Do you have enough information to determine the relative risk for lung cancer from asbestos exposure?
A. I have more information in that case, in that I did get a chance to look at the lungs, and that unlike Radon, I can see asbestos bodies if they're there. I didn't see any in this case. And although I don't have an adequate occupational history, I had no history of such exposure.
Not seeing any asbestos bodies, not knowing about any exposure, I thought asbestos probably had nothing to do with it.
Q. My question still has to do with assigning a relative risk to Mr. Little, do you have enough information to do that?
A. Yes, I think so, in that, I've got pieces of lung that were not affected by the radiation, that showed no evidence of asbestosis and no asbestos bodies, and the samples are not large, but they suggest to me that he

347

probably did not have occupational asbestos exposure of a degree adequate to produce lung cancer, because I think it takes a fairly heavy dose of asbestos to produce lung cancer.
Q. Okay. Well, you said that you could assign a relative risk in epidemiological terms. So what would his relative risk of lung cancer from asbestos be --
A. Mr. Little's risk?
Q. Right.
A. From what I've seen and what I know, I'd say his relative risk from asbestos exposure approaches zero, that asbestos did not have a role in the cancer.
Q. Are you aware that there is no such thing as zero relative risk, that one is actually the lowest relative risk that you can have in an epidemiological study, meaning --
A. Oh, relative risk.
Q. Yes. I'm talking from --
A. I was using it -- like I said, I'm not an epidemiologist -- I was using this in just general terms, that his increased risk, because of any exposure to asbestos, was minimal.
Q. Okay. And all of my questions are -- they have to do with epidemiology and the relative risk as used in epidemiological studies?

348

A. Okay. His relative risk from asbestos then was approximately one.
Q. And which of the studies would support that? And do you intend to -- first of all, we may save a lot of time, do you intend to offer any testimony on relative risk?
A. No, unless I'm specifically asked about what I think about his exposure to asbestos and lung cancer was.
Q. Okay.
A. In which case, I'll say that as a pathologist, I don't think there was any.
Q. Okay. If his deposition testimony or other work history records were contrary to that, would you have any reason to dispute his occupational exposures?
A. If you had a work history of asbestos exposure, I would take it into account and change it from, you know, virtually no effect to some possible effect. But from the standpoint of pathology, I don't think that there's a real increase in lung cancer until scarring appears which could be seen on x-rays, he had plenty of those, and which can be seen on the microscope at even lower doses, and I did see lung tissue with no evidence of that. So I don't think that asbestos played a role.
Q. Okay. And, again, I'm focusing on relative risk as used in epidemiological data. Do you intend to offer

349

any opinion whatsoever with respect to relative risks?
A. In the case of asbestos --
Q. In any aspect, including asbestos.
A. I don't think I'd have very much clout as an epidemiologist, but some of the work that I've done and been associated with over the years does have some fairly convincing epidemiologic evidence regarding asbestos and asbestoses and its relationship to lung cancer. So I might refer back to those.
Q. Actually, let me move to strike that as non-responsive.
My question was, do you intend to testify in this trial about relative risk from an epidemiological standpoint?
A. No; from a pathologic standpoint, yes.
Q. I'm talking epidemiology.
A. No.
Q. Are you qualified as an epidemiologist?
A. Absolutely not.
Q. Are you qualified to take epidemiological data and independently analyze it?
A. Only in the sense that any pathologist might be able to use that, and in the same sense that you might be able to use it. But from the standpoint of critical analysis as one epidemiologist to another, no, I can't do

350

that.
Q. Are you qualified to take a set of data from an epidemiological study that does not control for confounding factors, and control for confounding factors?
A. No.
Q. Would it be fair to say that, from an epidemiological standpoint, you do not know Mr. Little's relative risk of contracting cancer from risk factors other than tobacco smoke?
A. That's correct.
Q. Is it fair to say that, from an epidemiological standpoint, you do not know Mr. Little's relative risk of developing cancer after smoking for 20 years or 25 years, low-tar, ultra low-tar filtered cigarettes; is that correct?
A. I do not know precisely, no.
Q. Without speculating, could you testify, with a reasonable degree of medical certainty, that Mr. Little's relative risk from non-tobacco factors was greater than his relative risk from tobacco?
A. My own opinion is that his tobacco was the greatest known risk, because it's the only one I really know of that seems to have very much possibility of being real. But that's the kind of question that I think an epidemiologist should try to address.

351

Q. So in other words, for you to address that question, you would have to speculate; is that correct?
A. Right. And there's no information, and it's not the sort of thing I do.
Q. Now, in your report, you characterize Mr. Little's cancer as bronchogenic; is that correct?
A. I thought it was.
Q. And bronchogenic cancer is cancer that arises in the major airways; is that correct?
A. It arises in the bronchus, yes.
Q. And bronchus is?
A. It's an airway that has cartilage.
Q. So it's not -- it's something distinct and different than a bronchioli?
A. Right. The bronchioles are the very small ones; they don't have cartilage. But bronchi are the bigger ones that do have cartilage.
Q. Doctor, wouldn't you expect, for a tumor that arises in a bronchus, to obstruct breathing?
A. It would obstruct breathing in that bronchus, yes.
Q. Are you aware of any evidence that Mr. Little presented with any problems breathing?
A. No. And it -- in thinking back about this, his cancer didn't occur in a main stem bronchus. It wasn't in

352

the hilum of the lung; it was a little farther out. So any bronchus that was obstructed was not a big bronchus; it would have been a small one.

And the affects of a partial obstruction of the bronchus might have been something that he would have noticed in the form of a wheeze, whistle, something odd. I don't remember anything like that in his case.

Q. Okay. Can you direct me to what medical records or what specific evidence would suggest or support your opinion that Mr. Little's cancer arose in one -- in a bronchus?

A. I thought -- in fact, I remember at the time I was reviewing this material, looking at a section that had an airway in it that had some cartilage, and I'm thinking I imagine that's where it's from.

Also, there's the radiology, and this is something that the radiologist could do better than I could, pinpointing exactly where the center of the first biggest nodule was and its relationship to an airway.

I did not look at the gross specimen after the lobectomy, and it was altered by the radiation anyway. That would have been my preferred method of saying whether this is bronchogenic or not.

Q. And --

A. So I didn't have the very best material for

353

doing that.

Q. Let me ask you, you did look at his CT scans; is that correct?

A. Right. No, I did not look at CT scans.

Q. You did not look at CT scans?

A. No, I looked only at the reports.

Q. Oh, I'm sorry. You looked at the reports of the CT scans; is that correct?

A. Right.

Q. And you also looked at surgical operative reports; is that correct?

A. Right.

Q. If Dr. Reed reported that the bronchiole margin was negative for tumor, wouldn't that tend to suggest that it was not a bronchogenic?

A. No. When she takes out a cancer, she tries to get to a part of the bronchus that does not have any tumor remaining, so that she's not leaving any tumor.

If she has to cut through tumor, what she'll try to do is go back and keep moving up the airway until she gets to a place with no tumor, because she doesn't want to leave any tumor in.

Q. Okay. So when it says that bronchiole margin was negative for tumor, that just means that she has cut enough of it that no tumor remains by the bronchiole

354

margin; is that correct?

A. That's correct.

Q. Are you aware of any pathology report that would be taken where the tissue sample is designated as including part of a bronchus?

A. May I look back through these --

Q. Certainly.

A. -- and through my report and see what I say about this?

The difficulty in this report, I think, was the extensive radiation chemotherapy. It made even the gross description a little difficult. There are statements such as this one saying that the tumor approaches to within a tenth of a centimeter of the hilum; the hilar area of the lung is where the large airways and vessels are concentrated. So it's impossible to be in the hilum and not be in an area where there are bronchi. In fact, the bronchi extend out well beyond that.

Q. Not the bronchi, but how about the bronchus with the cartilage formation?

A. Those, yeah, they are in that part of the lung. So what this describes is a process that involves large airways.

It does not describe a discrete bronchus from which the tumor arises, partly because the tumor was

355

fairly large here, but more because there was so much necrosis and destruction that it -- those relationships would have been destroyed.

Q. Can you tell me what evidence you're relying upon for your opinion that Mr. Little's cancer was bronchogenic?

A. It's – the center of it appeared to be in the section of the lung where most lung cancers arise; it's close to the hilum.

This is not -- although it sticks out to the pleura and this pleural retraction, this is not one of those subpleural peripheral cancers that one often associates with bronchioalveolar or bronchioloalveolar origin. That's one factor.

Another factor is that I didn't see the pattern of BAC which –

Q. Sir, I'm sorry. My question is -- I don't mean to -- we've got still a lot to cover, and I don't mean to cut you off, but my question was actually just with respect to bronchogenic carcinoma. What evidence supports your opinion of bronchogenic?

A. Well, there are really only two reasonable places the tumor could come from; one is the bronchi, and the other is the bronchioles or alveoli.

Q. Okay.

356

A. So it's either a bronchogenic carcinoma like the average old lung cancer, or it's a BAC from the bronchioles and alveoli. The ones from the bronchioles and alveoli should have tumor cells that look like that.

Now, we run into the problem here that BAC is defined by its pattern of growth more than by the cell that it comes from. There's also the problem that you can get peripheral squamous cell carcinomas and so forth, that are solids and are not back BACs.

But this one seemed to be from the part of the lung where the bronchi were and had to involve the bronchi because of the size of the tumor. It could not not involve them.

Q. Isn't that correct, irrespective of where it originated, that if you've got a four-plus centimeter tumor, that's a tumor that's about the size of a lemon, right?

A. Right.

Q. Wedged in your lung, at a point of your lung where it's fairly narrow up at the left upper lobe, that just due to size --

A. It almost has to involve a bronchus.

Q. Correct, but that doesn't mean that it originated in the bronchus; is that correct?

A. Not absolutely.

357

Q. The only way to know that would be to have the tumor, to be able to cut the tumor and determine where the center of that tumor is; is that correct?

A. Yeah. Even that's not absolute. A tumor could grow in some eccentric fashion, but they don't usually.

The CT scans in the hands of the radiologist, looking at this specific question, CT scans taken before chemotherapy and radiation might be better able to answer this question better than a pathologist could, given the changes that happened in that lung.

MS. SCHMAHL: Actually, can we take a break please?

THE DEPONENT: Sure.

(A recess transpired.)

BY MS. SCHMAHL:

Q. Dr. Harley, do you agree that respiratory bronchiolitis is defined as an inflammation of the bronchioles?

A. Yes.

Q. Respiratory bronchioles are the smallest of the bronchioles; is that correct?

A. Yes.

Q. Just half a millimeter in diameter?

A. That's about right.

Q. And respiratory bronchioles connect with

358

terminal bronchioles to the alveolar ducts; is that correct?

A. Right, that's correct.

Q. Your expert report does not document respiratory bronchiolitis in your review of Mr. Little's December of 1995 pathology; is that correct?

A. Right.

Q. But you did see respiratory bronchiolitis in the pathology materials that were gathered in March of 1996; is that correct?

A. Yes.

Q. Did you also see respiratory bronchiolitis in the pathology materials that were gathered in September of 1996?

A. This was the large radiated specimen? That was too distorted to make sense of.

Q. Let me hand you what will be marked as Defendant's Exhibit 28.

MR. EVANS: I'm sorry; I think we are up to 30.

MS. SCHMAHL: Thank you, Defendant's Exhibit 30.

(DFT. EXH. 30, Ambulatory Care Pavilion Record dated 1/29/96, was marked for identification.)

359

BY MS. SCHMAHL:

Q. For identification, Exhibit 30 is an Ambulatory Care Pavilion record dated January 29th, 1996.

Let me refer you, briefly, to the second sentence under Interval History. It says there that the patient returns today in scheduled follow-up complaining of a cough, a temperature of 101 degrees, and a headache; do you see that?

A. I do.

Q. And Exhibit 35 -- excuse me, Exhibit 30 is dated one and a half months before the March 1996 pathology specimens were collected; is that correct?

A. Right.

Q. Directing your attention further down the page to the planned section; are you with me?

A. I am.

Q. Exhibit 30 states that Dr. Stuart placed the patient on antibiotics with Amoxicillin for ten days; is that correct?

A. Correct.

Q. Amoxicillin is an antibiotic, correct?

A. Correct.

Q. It's an antibiotic that is intended, in the context of this, to deal with the pulmonary or suspected pulmonary infection; is that correct?

360

A. That's right.
(DFT. EXH. 31, Ambulatory Care Pavilion Record dated 1/1/96), was marked for identification.)
BY MS. SCHMAHL:
Q. Doctor, you've been handed what has been marked as Exhibit 31 to your deposition. For identification, Exhibit 31 is an Ambulatory Care Pavilion record dated February 26, 1996.
Directing your attention to the third sentence in the section Interval History, it's probably a third of the way down the page. The third sentence states, The patient reports a dramatic improvement in his cough and sputum after taking Amoxicillin about three weeks ago; is that correct?
A. Right.
Q. So Mr. Little had taken Amoxicillin, and as of February of 1996, he reported a dramatic improvement, correct?
A. Right.
Q. If a patient, like Mr. Little, had a temperature of 101 and a cough, and those symptoms were resolved by an antibiotic such as Amoxicillin --
(The proceedings were interrupted.)
BY MS. SCHMAHL:

361

Q. -- would you agree that the patient had a respiratory infection?
COURT REPORTER: I'm sorry. Could you hold on a minute?
Mr. Booth, do you want a copy of the transcript?
MR. BOOTH: Yes.
COURT REPORTER: Thank you.
I'm sorry.
(Mr. Booth departed the deposition.)
MS. SCHMAHL: Could you read back the last question?
(The Court Reporter read the question commencing on page 360, line 21, and concluding on page 361, line 2.)
THE DEPONENT: Yes.
BY MS. SCHMAHL:
Q. Would you agree that the symptoms described in Exhibit 30 are consistent with a recent bout of pneumonia?
A. Or bronchitis, yes.
Q. Let me direct your attention to -- I believe you have in front of you Exhibit 22 to your original deposition, which is a surgical pathology report dated March of 1996?
A. 22, yes.

362

Q. Okay. Now, the treating pathologist who --
A. I'm sorry?
Q. I'm sorry. It should be September of 1996; is that correct --
A. That's correct.
Q. -- with label 22.
The diagnosing pathology who examined Mr. Little's right lower lung pathology in September of 1996, found that one of his tissue samples had, quote, changes suggestive of pneumonia; is that correct?
A. That's correct.
Q. There under the diagnosis section towards the bottom of the page. In fact, changes suggestive of pneumonia was Dr. Richardson's final diagnosis of that tissue sample; is that correct?
A. Right.
Q. Do you know whether Mr. Little had a history of pneumonia prior to his lung cancer diagnosis?
A. No, I don't know.
Q. Have you see any records relating to Mr. Little where he did have a diagnosis of pneumonia?
A. I've seen the records. It's been a long time since I've reviewed them, so I don't remember whether he had episodes of pneumonia. I wouldn't be surprised if someone was to have occasional episodes of pneumonia.

363

Q. At least as of Dr. Richardson's pathology report in September of 1996, he had changes in his lungs suggestive of pneumonia, correct?
A. Right.
Q. Would you agree that respiratory bronchiolitis is often associated with pneumonia?
A. That's a bit of a jump. The term "pneumonia" is being used in different ways here. The first one there in February, was really probably bronchitis. It was an acute thing; he had a bacterial infection that responded to antibiotics. Involvement of his lung was not entirely clear. He didn't have rals then; when you listen to his chest, his chest was clear.
This one in September is later on, after radiation and so forth, and people -- and he had a large lung cancer which had been removed and would have had some obstruction and all sorts of things happening. It's a setup for pneumonia. What's described here is focal fibrosis changes suggestive of pneumonia. If it had been a frank, obvious bacterial pneumonia, she would have called it that.
So what she's seeing is a confused pattern. Fibrosis is the end result that the inflammation, it would have taken weeks or months. And she's seeing a confused pattern of response to something. And that may or may not

364

have anything to do with respiratory bronchiolitis.
Respiratory bronchiolitis is associated with cigarette smoking, usually. Cigarette smokers have more bronchitis, acute and chronic, and more pneumonia. So there will be a relationship there, but it's all indirect.
Q. Would you agree that Stedman's Medical Dictionary is an authoritative work?
A. Modestly.
Q. Are you aware of medical literature that does associate and, in fact, specifically states that respiratory bronchiolitis is often associated with pneumonia?
A. I'm not specifically aware of that. If I saw that, I would have to interpret it based on what the people were really talking about.
Respiratory bronchiolitis could actually be defined as a pneumonia if one wanted to. Pneumonia is a fairly general term meaning inflammation of the lung.
Q. Well, would a respiratory infection such as bronchitis, couldn't that result in inflammation -- as inflammation of the bronchioles?
A. It could; it frequently does. The common form of bacterial pneumonia is called bronchopneumonia; it involves the bronchioles and the adjacent lung. It's, oftentimes, centered on the respiratory bronchioles, and

365

even though it's an inflammation and an "itis" and you have to call it respiratory bronchiolitis, one can't do that anymore, because the term "respiratory bronchiolitis" has been taken out of context and now means this thing with the macrophages that we talked about earlier.
The kind of thing you're talking about would not necessarily have macrophages; it would have neutrophils. It's a different kind of inflammation. I know this sounds strange, but it's not really the same thing.
Q. So sitting here today, you can testify -- can you testify, with a reasonable degree of medical certainty, that what you term respiratory bronchiolitis was caused by cigarette smoking and not by a non-neoplastic lung infection such as bronchitis or pneumonia?
A. It could have been caused by those things and a variety of things. It did not have to be caused by cigarette smoking.
Q. Now, respiratory bronchiolitis, itself, doesn't cause lung cancer; is that correct?
A. No, it does not.
Q. And lung cancer doesn't arrive from respiratory bronchiolitis?
A. No.
Q. And the presence of respiratory bronchiolitis is

366

not indicative of cell type; is that correct?
A. Correct.
Q. And people can have respiratory bronchiolitis and it's not necessarily a predictor for cancer; is that correct?
A. Correct.
Q. Doctor, have we fully discussed Exhibit 6, which is your expert report?
A. I think so.
MS. SCHMAHL: As a matter of housekeeping, let me mark and introduce what will be Defendant's Exhibit 32.
(DFT. EXH. 32, Statement of Opinions, was marked for identification.)
MS. SCHMAHL: Off the record.
(Off-the-record conference.)
BY MS. SCHMAHL:
Q. Just briefly, for identification, Defendant's Exhibit 32 is your expert disclosure; is that correct?
A. Correct.
MR. EVANS: Let me just clarify that. It is a portion of the expert disclosure. It appears to be missing the witness' CV from -- which would have been at the front and the witness' actual report that we've been discussing, which would

367

have been at the back.
BY MS. SCHMAHL:
Q. Okay. Exhibit 32 consists of Appendix B (1), Appendix B (2), Appendix B (3), and Appendix B (4), which is your reliance list, correct?
A. Right.
Q. And in addition to what's been marked as Exhibit 32, there was Appendix A, which was your CV, which has not yet been – okay.
It would be Appendix A, which is your CV, and that has not yet been marked into evidence. And Appendix C would be your expert report, which was marked into evidence as Exhibit 6.
(DFT. EXH. 33, Appendix A, Curriculum Vitae, was marked for identification.)
BY MS. SCHMAHL:
Q. Defendant's Exhibit 33 is Appendix A to your expert opinion, a copy of your CV dated May 4th, 1999.
Have you updated your CV since May 4th, 1999?
A. I don't believe so.
Q. In addition to your -- what is actually written in your expert report of Exhibit 6, you also rely on some information contained in Dr. Hammar's expert report; is that correct?
A. Correct.

368

Q. You testified during your last deposition, I believe, that you were relying on two things from Dr. Hammar's report. The first thing is his conclusion that Mr. Little did not have BAC, correct?
A. Right.
Q. And the second thing you're relying on from Dr. Hammar's report are the results of the apoprotein surfactant and the thyroid transcription factor 1 test; is that correct?
A. Right.
Q. You were not relying on any of the other stains that Dr. Hammar performed; is that correct?
A. That's correct.
Q. And you are not relying on any of his other conclusions or analyses; is that correct?
A. That's right.
(DFT. EXH. 34, Letter from Charles Patrick to A.J. Singleton dated 3/10/00, was marked for identification.)
BY MS. SCHMAHL:
Q. Let me hand you what has been marked as Exhibit 34 to your deposition. For identification, Exhibit 34 is the March 10th letter from Charles Patrick, an attorney at Plaintiffs' law firm, to A.J. Singleton at -- an attorney for R.J. Reynolds.

369

Have you seen this letter before today?
A. I don't believe so.
Q. Okay. Directing your attention to the first line. Charles Patrick writes that Dr. Russell Harley suggested that we have immunohistochemical stains performed to provide additional information as to the cell type of Martin Little's lung cancer. He, meaning Dr. Harley, stated that he did not have the appropriate materials for the necessary immunohistochemical stains readily available in his laboratory, and he suggested that we should send the pathology, slides, and blocks to Dr. Hammar for immunostaining.
Is the first paragraph of Mr. Patrick's letter an accurate statement of how Dr. Hammar became involved in this litigation?
A. I think so. As I remember it, this has been a while back, but I think what I said was that if he wanted to pursue this further, that I couldn't do the stains, and that there were -- that the stains were available at various places and maybe somebody else could, and might have suggested Dr. Hammar, because he has access to a lot of these things.
Q. When you say "if you want to pursue this further," is it your understanding of what was being pursued is demonstrating that the cancer was not BAC.

370

A. Right. I didn't think it was all that important to do this, because BAC is defined histologically on how it looks, and this doesn't look like a BAC to me, and it didn't to Dr. Hammar, and it didn't to Dr. Roggli, and it didn't to our pathologist here. So I didn't think that was a major thing, but I thought it might be of some interest.
I was sort of interested myself, because I don't have these stains available to me, and I didn't know exactly how they'd turn out.
Q. Briefly, what were the necessary stains that you did not have available in your lab?
A. The thyroid transcription factor is one that I could get; it was commercially available. The surfactant apoprotein stains were available in some places, but I didn't have any experience using them, and I like to use immunostains for awhile myself in my own setting before I start to trust them.
I've had long experience with surfactant, itself, and as a matter of fact, might have made the first antibodies to it, although I'm not sure what component I made them to, when I was a medical student.
But these particular stains were things that were a little difficult for me to get, and I hadn't had any experience in using firsthand, so I thought they'd be

371

better done in someplace where people were used to them.
Q. Could you have obtained the apoprotein surfactant?
A. If I'd worked on it, I could have probably.
Q. Could you have conducted the staining yourself?
A. Well, yeah, if the material -- if I have the material, it's an easy thing to do from that point on. Interpreting is another matter, because sometimes you get a stain that says this is a very specific stain; it stains only thus and such. And then you use it for awhile, and it turns out it not only stains thus and such, but this and that, and that and that and that; it becomes nonspecific. And I didn't have the background to feel that I'd be the best person to do this.
Q. Were the only two materials that you thought were appropriate and necessary for the immunohistochemical staining, was it simply the thyroid transcription factor 1 and the apoprotein surfactant A-1?
A. I think the surfactant was what I suggested, and I said there were other stains that can be used for these same purposes. And the two that Dr. Hammar ended up with, apparently, were these two.
Q. Now, why did you recommend Dr. Hammar, in particular?
A. I'm not sure I did. I think I said somebody

372

else. And I know Dr. Hammar right well, and I know that he has worked on various cases with this law firm and that they knew his phone number, same thing with Dr. Roggli.

And I think I said that there were other commercial entities where these stains were available. I think I mentioned Impath as one, so I'm not sure exactly how that worked out after that.

Q. Have you, personally, ever sent pathology materials to Dr. Hammar for his analysis for purposes of making a clinical diagnosis?

A. I'm not sure. I may have. He has considerable expertise in certain aspects of lung cancer, especially electron microscopy of lung cancer. That's not something we do very much anymore, and it's been a while.

I don't send a lot of material out, and I may have sent a case or two to him over the years, but I don't do it very often.

Q. So perhaps a case or two over the years?

A. Right.

Q. Other than Mr. Little's pathology, have you ever sent pathology materials to Dr. Hammar for his review or analysis in a litigation setting?

A. Again, possibly so. And if so, it would have been in one of the asbestos cases, because he has done a lot of work on that.

373

Q. Do you know what Dr. Hammar was asked to do by Plaintiffs' counsel?

A. No.

Q. Did you have any discussions with Dr. Hammar, as far as the staining or what he was asked to do with the pathology materials?

A. No.

Q. Did Dr. Hammar perform any stains that you did not suggest?

A. The thyroid transcription factor I don't think was one that I suggested. I think I left it sort of open, saying that there were other stains. And TTF was something I knew about, but I don't think it was something I would have said, do this. And besides that, I don't think I would presume to tell Dr. Hammar exactly what to do.

Q. So the only suggestions that you made to Plaintiffs' counsel with respect to -- can we call it IHC staining since it's so much easier to say than immunohistochemical?

A. Sure.

Q. The only suggestions you made to Plaintiffs' counsel with regard to IHC staining had to do with doing a surfactant stain; is that correct?

A. Right.

374

Q. And you mentioned, then, that there are other stains that could done on this pathology material; is that correct?

A. Right.

Q. Without specifying what those other stains are; is that correct?

A. Right.

Q. Were you aware that Dr. Hammar's lab did not have the apoprotein A-1 surfactant stain?

A. No, but it's a matter of finding somebody who has them. These stains all start off as research projects. Somebody purifies a protein. That's the hard part.

Once the protein's pure, then they can polyclonal or monoclonal antibiotics to it. It's not so hard to do; it's more standard. Once those are made, then anybody can do it.

Q. Were you aware that Dr. Hammar actually sent the pathology materials out to Dr. Gown's lab to be stained and analyzed?

A. I did get a report, at some point, saying what the results were and where they had been sent. These were not people that I knew.

Q. So you have never dealt with Dr. Gown?

A. No.

375

Q. Have you read any literature that he might have published on IHC staining?

A. I may have, but the name did not ring a bell.

Q. Do I take it, then, that you have never sent any pathology materials to Dr. Gown or his lab for staining or testing?

A. That's correct.

Q. Is it correct that the reason that you and Dr. Hammar did not have the apoprotein surfactant that was used in this case is that it's not commercially available?

A. That's the reason I didn't have it. If the things are not commercial available, it's hard to get. There are surfactant proteins that have been on the market off and on over the years. Like I say, I hadn't used them personally and don't like to use them until I've had some experience with them. I don't like to try and interpret them.

Q. And isn't it correct that when you wrote the "Histochemical and Immunochemical Methods of Use in Pulmonary Pathology," which is the chapter in Stephen Spitzer's (ph) book, Histochemistry and Pathology Diagnosis, surfactant-related apoprotein stains were not commercially available then; were they?

A. That's correct.

Q. And that book was written in 1987?

376

A. I'm not sure; if that's what my CV says, then that's right.
Q. So in the 13 years since your chapter was written, the surfactant apoprotein stains have still not become commercially available; is that correct?
A. I think they are commercially available now. I'm not sure exactly which ones, I have not asked the lab here to order them. They're expensive, and they need to be used a good bit in order to be justified.
Q. Let me ask you, is it your understanding that "commercially available" means that it has been approved by the FDA?
A. No. It just means that you can look them up in the IHC books and buy them. The FDA will not approve these things for many purposes, so it's up to the experience of the doctor who's using them to say whether or not they're useful in his own methods and practice. And that's why I like to have them around and play with them and so forth before I would tend to trust them.
Q. Is it correct, though, that a non-FDA approved IHC cannot be used to diagnose cancer in a patient?
A. It can't be used to diagnose it, but it can be used as a helpful tool, to provide more information for the person to consider in arriving at a diagnosis.
For instance, if one applies a

377

surfactant-related antibody to tissue, say in this case, where you have some tumor here and some bronchioles over here and some alveoli here, you can see type 2 cells, and you can see bronchiolar cells, and you can see tumor cells. If, in that slide, the bronchioalveolar cells stain, the type 2 cells stain, and the tumor cells don't stain, you say, Well, it's not acting like the type 2 cells and the bronchioalveolar cells in this case and in this slide.
For me to consider using that information in any diagnosis on an actual live patient, I would want to have seen those patterns a number of times before I place any trust in them. And then I don't make the diagnosis based on how the stains were; it's based on the whole picture and more on just the H & E histology. That's the background of histopathology.
Q. Would you agree that before IHC tests are approved by the FDA, there are numerous criteria that they must satisfy; they must be labeled with directions for use in performance claims? Is that correct?
A. Right.
Q. They must be tested in scientific studies; is that correct?
A. Yes.
Q. They must undergo the FDA's risk-based

378

evaluation; is that correct?
A. For immunostains?
Q. For any product submitted to the FDA, including IHC stains.
A. Well, at least that refers more to things that are applied to people. It's not like you're putting this on a person's skin or anything, but, yes.
Q. And, finally, they must withstand the scrutiny of the scientific reviewers at the FDA's Office of Device Regulation, correct?
A. Right.
Q. Surfactant apoprotein has never met those FDA requirements, has it?
A. No.
Q. Do you know whether the makers and creators of surfactant apoprotein A-1 have even applied to the FDA for approval?
A. I have no idea, probably not.
Q. Do you know whether surfactant apoprotein A-1 was exempt from FDA regulation because it was part of an investigational study?
A. The -- I'm sure that it started as an investigation; that's how all of these start.
Q. But my question is, do you know whether it was exempt from FDA regulation because it was being used in an

379

investigational study?
A. I doubt that an application for exemption would ever have been used. It probably would have been used in -- I don't know how this stuff was used. You'll have to ask the people in the laboratory that used it.
Q. So your answer to it would be no?
A. The answer to it is, I don't know.
Q. Okay. Now, let me ask you, in your practice here at MUSC, have you ever used a non-FDA approved IHC to diagnose a patient with cancer?
A. I think every modern pathologist in the country uses non-FDA approved immunostains, but they're not used for making the diagnosis. That has happened a time or two, and it's a terrible mistake to try to do that. One can't trust the immunostains to make a diagnosis, but they can be used just like any other stain, to provide a little information and push one's opinion this way or that.
Q. And the reason that they can't be used to make a diagnosis is that the results are not consistent; isn't that correct?
A. Consistency is part of it, and they need to be used over a wide variety of test cases before enough is known about what they do and don't do.
Q. For example, an IHC stain could give you information if you know that 75 percent of a cell type

380

stains positive for that particular stain, correct?
A. Right. In the case of mesotheliomas, for instance, we do this all the time. Is it mesothelioma or is it adenocarcinoma? And there are immunostains that stain adenocarcinoma and tend not to stain mesothelioma, but they don't stain all the adenocarcinomas, and they occasionally stain mesotheliomas.
If you use one of them, it gives you a little hint. If you use two of them, that's a little more helpful. If you use three of them, you can get up to the point that -- there's studies that can be done that show that they're 95 percent accurate in categorizing. But even then, there's room for doubt.
Q. Because, again, the IHC stains demonstrate tendencies, correct?
A. Yeah. They are -- they can be quite specific for certain things. There are some that are far better than others.
The prostate specific antigen is one we use all the time. It's almost never a positive in anything except prostate cancer. However, I've seen it stain mesothelioma in frozen sections, which is surprising, but nobody would ever think to look for that.
And so even in the ones that -- even in the best ones, they can be trusted under the usual circumstances to

381

some degree.
Q. So they can be trusted to help support what you already saw under the microscope; is that correct?
A. Right, or to not support, to make -- more often they do that, raise questions, make a person a little less certain; in which case, you go back and try to find something else and try to reflect the degrees of certainties and uncertainties in reports.
Q. Are you aware of any medical literature that would discuss the degree of certainty of the results from an apoprotein surfactant and a thyroid transcription factor 1 test?
A. I am aware of some, but I don't know what the names are. There were one or two at the United States, Canadian Academy of Pathology meeting in New Orleans recently, and they're starting to pop up. These are things that people are interested in. I think there will be more of them in the near future.
Q. Do you have any opinion as to the level of certainty?
A. As to how accurate and good these are?
Q. Right, when you take the two and combine them.
A. No, I don't know.
THE DEPONENT: Do you mind if I make a phone call? Excuse me a moment.

382

(A recess transpired.)
(DFT. EXH. 35, Summary of Dr. Hammar's Immunohistochemical Staining, was marked for identification.)
BY MS. SCHMAHL:
Q. Madonna has handed you what is Exhibit 35 to your deposition. For identification, Exhibit 35 is a chart entitled Summary of Dr. Hammar's Immunohistochemical Staining.
To your knowledge, is Exhibit 35 an accurate summary of the stains Dr. Hammar performed?
A. To my knowledge, it is.
Q. Would it help you to compare Exhibit 35 to Dr. Hammar's report?
A. If I wanted to be absolutely sure, I think I would have to, because I don't remember all of this.
This seems to be accurate. It's a little confusing, I might miss something, but I think it's accurate, the chart.
Q. And that is after comparing Exhibit 35, which is the chart with Exhibit 35 (sic), which is Dr. Hammar's expert report; is that correct?
A. Correct.
MR. EVANS: Exhibit 5, which is Dr. Hammar's report.

383

MS. SCHMAHL: Thank you.
BY MS. SCHMAHL:
Q. Why are you only relying on the apoprotein surfactant stain and thyroid transcription factor 1 stains when Dr. Hammar did a total of nine stains?
A. The other stains are not things that I necessarily would have had a question about.
Q. Would you say --
A. And the meanings of these stains in Dr. Hammar's hands, I'm not sure how he interprets these.
Q. So in your opinion, are the other stains listed on Exhibit 35 not relevant to a determination of cell type?
A. They could be. They were not things that I thought would be especially helpful in the differential that I had or that seemed to be coming up in this case, which was not originally my differential.
The synaptophysin and chromogranin stains, for instance, are not things that I would have thought to do, because they're usually used in looking for neuroendocrine, usually small cell carcinomas; and these had no features of those, so I wouldn't have thought to do that.
However, I know that in some cases, of non-small cell carcinomas, those stains can be positive, in which

384

case they're called large cell carcinomas, or something or other, adenocarcinomas, whatever they turn out to be, with neuroendocrine markers. And those don't seem to have a great deal of significance in response to therapy or predicting how the tumors are going to react in the long run.

Q. Okay. How about --

A. So I wouldn't have done those, but they might show some interesting information. In this case, they didn't.

Q. How about the cytokeratin, what would those normally be used for, briefly, please?

A. There are a lot of different kinds of cytokeratins, and they come in low, medium, and high molecular weights, and are expressed more strongly in one kind of cell than in another, and sometimes in different locations in the cells next to the nucleus, or more peripherally in the cell, and can be useful in subcategorizing some of these types of tumors.

My experience with them, in general, has been that there's so much overlap in the responses, that I don't get very much useful information in a case like this.

The CK 7 is one that's usually positive, for instance, in lung cancers, and is usually not positive in

385

metastatic cancer from the colon. So if I had a question of whether this is an adenocarcinoma from the lung or the colon, that might be one of the stains that I'd do.

But there's not a lot of circumstances in which I find the differential a strong enough factor for me to use them all that often. I used to use them a lot, but I don't use them very much anymore.

Q. Would you agree that with a low-molecular-weight keratin and a high-molecular-weight keratin, that there's a great deal of overlap in the results between cell types?

A. That's what I find.

Q. Would you agree that, if I'm summarizing your previous testimony correctly, the same is the case with the cytokeratin stains, that there's a great deal of overlap between the cell types of non-small cell cancer?

A. In lung cancers, yes, there is, it's been my experience.

Q. Using the cytokeratin stains?

A. Right.

Q. So staining, positive or negative, using cytokeratin does not provide a great deal of helpful information as to what the classification of the tumor is; is that correct?

A. That's correct.

Q. Can you tell me what the Movat's Pentachrome is,

386

what's that designed to test?

A. It's a connective tissue stain that is most useful for bringing out patterns. And I don't use it for cancers very often at all. I use it all the time for inflammatory lung conditions, for bringing out patterns of the lung, so that if the lung is changed by fibrosis and scarring, I can see through that and see what the lung used to look like to some extent.

It has in it an elastic stain, which is very useful in the lung because the lung is so full of elastic. It has a mucin stain in it, either an alcian blue or an alcian green.

COURT REPORTER: I'm sorry; a what?

THE DEPONENT: A-l-c-i-a-n, blue or green, that will stain mucous those different colors. So if there's an adenocarcinoma, it could stain the mucin in the tumor, which would indicate that it's an adenocarcinoma.

But I don't use the Movat for that particular thing very often. It's got stain for collagen and red cells and muscle and so forth. It's a very colorful, pretty thing.

BY MS. SCHMAHL:

Q. But you would not use the Movat's as your primary stain for determining whether a cell has mucin or

387

does not have mucin; is that correct?

A. It's more complicated than one needs for that particular question.

Q. Do you agree that approximately 75 percent of adenocarcinomas stain positive for thyroid transcription factor 1?

A. I really don't know. I haven't had experience with that stain.

Q. Have you had no experience with thyroid transcription factor 1?

A. I've only read about it. I've never done one.

Q. So would it be fair to say, then, that you are relying on Dr. Hammar's opinions and analysis concerning the significance of any of the thyroid transcription factor 1 testing?

A. In this case, yes, the descriptions are nice and clear, that the alveolar cells and bronchioalveolar cells are staining within -- that's what it's supposed to do -- and the tumor is not, so it doesn't seem to be staining like those particular cells in this particular situation.

But I don't have personal experience with that stain.

Q. Do you have enough experience with that stain to have an opinion as to whether TTF-1 staining can be positive in large cell carcinomas?

388

A. No, I don't know.
Q. Do you have an opinion as to whether the F-4 reactive cells and F-5 reactive cells staining positive with TTF-1 support or undercut a diagnosis of adenocarcinoma in this case?
A. I think they provide a little information against origin and bronchiolar cells or alveolar type 2 cells, but that's not definite. And I don't know how they stain the usual large cell or the usual types of adenocarcinomas in the lung.
Q. Did you actually examine the slides that Dr. Hammar did the immunochemical staining on?
A. No.
Q. Did you look at photomicrographs --
A. No.
Q. -- of the slides?
A. No.
Q. So you're simply relying on what is actually written in Dr. Hammar's report; is that correct?
A. Right.
Q. Do you have any opinion as to whether the thyroid transcription factor 1 staining is a more specific marker for adenocarcinoma than lung surfactant proteins?
A. For adenocarcinomas in general?
Q. Yes, sir.

389

A. I really don't know.
Q. Do you have an opinion as to whether surfactant apoprotein A-1 can be positive in adenocarcinomas?
A. Well, I'd be surprised if it weren't positive in some of them.
Q. Do you have an opinion as to whether BACs with type 2 pneumocytes are more or less likely to stain positive for lung surfactant proteins?
A. I would be surprised if they were not more likely to stain. I would expect them to stain with that in most cases.
Q. Would you expect BACs with Clara cell to generally stain negative for lung surfactant proteins?
A. I would imagine that they would occasionally be positive, but that the interpretation of what the cell type was would be influenced by whether it stained like that. If it didn't stain, you'd tend to say it was not a type 2 cell. And if it did, you'd say it was. And it might have features of both Clara cells and type 2 cells, so there would need to be some stains for Clara cells as well to answer that.
Q. And to the best of your knowledge, have there been any stains for Clara cells performed on Mr. Little's pathology?
A. Not to my knowledge.

390

Q. Do you know the name of the stain that would test for the presence of Clara cells?
A. No, I don't know of really reliable stains for Clara cells. There are a number of things that do stain them. Their appearance, the way they grow, is one of their characteristic features, and they have some electron microscopic characteristics as well.
Q. And what Dr. Hammar called the reactive alveolar lining cells, the surfactant apoprotein A-1 did stain positive; is that correct?
A. Right.
Q. What significance do you attach to that finding?
A. It supports the concept that the stain works and that it's staining what it's supposed to, because that's where it should be found.
Q. Can you clarify that?
A. That the surfactants produced by type 2 cells, these are bigger, more active type 2 cells, probably more surfactant, and they ought to stain nicely with it, so they do.
Q. Okay. And they did in this case, the F-4 reactive and F-5 reactive?
A. I think that's what's being described here.
Q. How do the results of the apoprotein A-1 testing support your opinion as to cell type or causation?

391

A. They don't stain the tumor. They do stain reactive type 2 cells. That's some evidence.
That's pretty good evidence that the tumor cells are not producing surfactant. That doesn't necessarily mean that they aren't some kind of bronchiolar cell that could grow like a BAC.
But the BACs are really defined, at present, not by stains which would indicate their cell of origin, but by the pattern of growth, it's how they grow.
For instance, there are -- one of the types of BAC is a mucinous type, in which mucinous cells produce mucin, and there's no cell that looks like that in the normal bronchiole or the normal alveolus; yet this is termed a type of BAC because of the fact that it grows along the alveolar walls.
So it doesn't provide any absolute answers, but if it had stained the tumor, it would have given me more pause to think, could this have originated in an alveolar type 2 cell? But even so, for it to be what we traditionally call BACs, the things that have a background of statistics, which I can't talk about, bearing on tobacco relationship, it's still not defined that way by the cell of origin; it's defined by the pattern of growth.
Q. Okay. Would you agree that the positive staining in the reactive cells would tend to be supportive

392

of an adenocarcinoma?
A. I don't think it has any bearing on that.
Q. Okay. Would you agree with the statement that adenocarcinomas are identified by gland formation and/or mucin production in the form of intracytoplasmic vacuoles?
A. That sounds like a direct quote from me.
Q. Would you agree with that statement?
A. And I still agree with myself on that one.
Q. Doctor, is it common in the field of pathology to do mucin stains on pathology to determine if the tissue is an adenocarcinoma?
A. It is commonly done. It's not done across the board. It's considered unnecessary for practical treatment purposes. The statement is often made that it's not recommended that we do mucinous stains on every tumor, but it is very commonly done. I do it frequently.
Q. But for purposes of determining -- in the treatment context, it's not necessarily important to know whether it's an adenocarcinoma; is that correct?
A. Adenocarcinoma versus large cell, the adenocarcinomas that you can only tell that's what they are, by doing a mucin stain, act the same way as if they didn't have the mucin, so that it doesn't make any difference for treatment purposes. So I think that's why it's recommended they not be done. They don't cost all

393

that much, but it doesn't seem to help.
Q. Because what really matters, is it small cell or is it non-small cell, is that correct, for treatment?
A. That and for purposes of prognosis. If it's BAC, the prognosis is a little different. If it's squamous, the prognosis is a little different. If it's a solid adenocarcinoma or a solid large cell carcinoma, the prognosis is about the same; the response of treatment is about the same.
Q. But in situations where the subclassification of the non-small cell cancer is important, mucin stains are recommended as a stain to determine whether it is an adenocarcinoma or not, correct?
A. Right.
Q. Does the World Health Organization still recommend the use of a stain containing alcian green mucin?
A. I doubt it. The Europeans were really the ones that started doing that originally, and Americans tended to use alcian blues. And there are a fair number of labs in this country that used an alcian green, just because it was there.
Blue and yellow make green. There's an alcian blue; there's an alcian yellow. If you add the two together, you get a green, and that's really what alcian

394

green is. So I think we just tend to use alcian blues.
Q. Is that what you use here at MUSC when you need to determine whether it's an adenocarcinoma by staining?
A. We use that, we use a PAS stain, and there are a few others we use, mucicarmine stains.
Q. Could you list all the stains that you are aware of that you use here at MUSC to determine whether there is mucin production in a tumor. You've already mentioned alcian blue, the mucicarmine. What is the PAS is that the periodic acid shift distaste (sic)?
A. Diastase.
Q. Diastase.
A. Right. That's one that's very commonly used, and I think the only other one we use commonly -- it's not too common -- is a Hale's colloidal iron stain.
I think for practical purposes, the alcian stains, the PAS, and the mucicarmine are the things that people generally use.
Q. Tell me if you still agree with this statement. Undifferentiated large cell carcinoma may be regarded in some cases as a failure of classification, a garbage can class of epidermoid and adenocarcinomas lacking the specific features needed to differentiate between them.
Would you agree with that?
A. Sometimes I think that's the case.

395

Q. Would you agree with this statement: Given additional materials, such tumors usually prove to be adenocarcinomas.
A. I think they turn out to be adenos more often than anything else.
Q. And one of the ways to determine if they were adenocarcinomas would be to do one of the mucin stains; is that correct?
A. Right.
Q. Would you agree that in situations where you do not have a large amount of pathology material available for histological examination, that a mucin stain would be the next most reliable indicator of whether it was adenocarcinoma or not?
A. I think so.
Q. To your knowledge, has any mucin testing or staining been done on Mr. Little's pathology materials?
A. I don't remember one. I see here that there was a Movat that was done.
It simply says done. It doesn't say if there was any mucin found or not. I guess there wasn't. It did not look like the kind of tumor that would produce mucin. You can't always tell by looking at them with an H & E.
Q. Because when, for example, you looked at the September 1996 pathology, you saw something in the

396

pathology that appeared to be a gland formation or a gland that was trying to form; is that correct?
A. Right.
Q. And it would be -- would it be those types of glands that form the mucin?
A. Well, the glands can accumulate mucin, but as from the statement you read earlier, I like to see the tumor -- I like to see the mucin within the cytoplasm of the tumor cell itself, just to prove that it didn't come from some adjacent source.
Q. Is there any way to see the mucin in the cytoplasm of the cell itself without using a mucin stain? Can you just see it histologically?
A. Sometimes, but frequently you cannot. And one of the main reasons for not doing this stain, as I've said earlier, is that it just doesn't seem to make any difference as far as treatment and prognosis. So I think that's the reason people don't do so many of them as they used to.
Q. But you do realize that in the context of Mr. Little, all the staining that has been done is not for treatment, but for the purposes of litigation; is that correct?
A. I think -- well, this staining has been done because of the litigation.

397

Q. And you're referring to Dr. Hammar's staining, correct?
A. Right. The other stains that were done, I'm not sure what all was done. I remember the CEA, because I took a picture of a negative CEA; that was done.
Q. Let me clarify then. Dr. Hammar's staining was not done for any sort of treatment purpose; is that correct?
A. Right.
Q. Simply for litigation?
A. That was done for purposes of classifications because of litigation issues, yes.
Q. And do you realize that the issue with classification is Defendant's contention that Mr. Little had an adenocarcinoma, correct?
A. Right.
Q. Specifically, that Mr. Little had a BAC; is that correct?
A. Right.
Q. Would you agree that it would be reasonable, if you're trying to determine whether a tumor is or is not an adenocarcinoma, to do a mucin stain?
A. It wouldn't hurt. It's an easy thing to do.
The reason that I'm saying it's not a BAC is not because it does or does not have mucin, because it doesn't

398

grow like one. If it grew like one and if I wanted to know whether it was the mucinous type, I could do one; although in the case of BACs, that really is obvious on an H & E because you have these tall cells that have a goblet appearance, goblet cells more or less. And it's not even necessary to do the mucin stain to call it a mucinous type adenocarcinoma with a BAC.
If it's not a BAC, but if you still want to know whether it's an adenocarcinoma, it would be a reasonable thing to do.
Q. Okay. So the answer to my question is, yes, if there is an issue as to what a tumor is, whether it is or is not adenocarcinoma, then doing a mucin stain would be the way to obtain that information; is that correct?
A. That would be the sensible thing to do.
Q. Okay. And would it not also be a sensible thing to do in the context of pathology material that is simply diagnosed as large cell carcinoma?
A. If one wanted to try to differentiate between large cell and adenocarcinoma, it would be a reasonable thing to do. In fact, that is one of the main reasons for doing it.
Q. Because as you, yourself, have written, most undifferentiated large cell carcinoma with additional testing will prove to be adenocarcinoma; is that correct?

399

A. Right, and that's with small amounts of tumor. We didn't have large amounts here, but everything seemed to be solid.
So I guess doing a mucin stain didn't seem to be anything that anybody thought of as being needed. It's interesting that that is one of the components of Movat's, and that Dr. Hammar did it. I don't see that he said anything about mucin.
I haven't got his report here still, do I?
Q. But now you said that --
A. Like I said, if he were looking for mucin, I don't think he would have done a Movat, he would have done an AB, PAS, or something like that.
Q. Correct.
Dr. Harley, at least with respect to the pathology sample that you took the photomicrographs of, and I'm specifically referencing slide 18-2, where you suggested that the tumor was supposed to be making glandular space, and when I asked you if, in your definition, that's suggestive of an adenocarcinoma, you stated that it was suggestive of an adenocarcinoma; is that correct?
A. Right. That's something that I didn't really appreciate when I first looked at this, and then in reviewing these photographs in such detail, it did seem to

400

be more obvious, and I know that -- I notice here that Dr. Hammar, at one point, said he found features consistent with adeno squamous at one point.

Q. And actually --

A. So it does seem to have some features that would make one wonder about that.

Q. And at least with respect to the September 1996 biopsy material, that is one of those very small samples that you discuss in your book as being potentially adenocarcinoma with more materials or with further testing, correct?

A. Correct. That is a small fragment of tumor.

Q. Okay. Now, would you have considered doing a cytokeratin 13 stain on Mr. Little's pathology materials?

A. Not offhand. I'm not even sure whether a cytokeratin 13 stains.

Q. How about a cytokeratin 17?

A. Same thing, it's not one that -- that's one of the new cytokeratins, and I haven't had very much personal experience with those.

Q. How about the CD-44-S stain?

A. That didn't occur to me. I use that occasionally, but wouldn't have especially thought of doing it here.

Q. How about the CD-44-V6 stain?

401

A. I think that has another name. I'm not sure what it is. A lot of the immunostains have more than one name, and they get called by a certain name in one institution and by another name in another one and they're the same thing.

So I'm not sure exactly which CD-44 that is, and I'd have to look at our stain sheet and see if that fits as to anything I want to use, but it's not something that, offhand, I would have thought of using in this case.

Q. Okay. How about a collagen 4 stain?

A. That sounds like something that Dr. Barsky would like to use. I may not know enough about the reactions of the different types of collagen, seeing whether or not basement membrane type collagen has accumulated in the middle of the tumor and so forth. That is the sort of thing that he's famous for. And it's not one that I do routinely. In fact, I may never have done it in a case of lung cancer, although I read about it occasionally.

Q. Would it be fair to say that there isn't any IHC stain or any stain of any type that will tell you the cause of a lung cancer?

A. That's true.

Q. Likewise, there is no staining that can be done to a cancer cell to determine if a patient was, in fact, a cigarette smoker; is that correct?

402

A. That's correct.

MS. SCHMAHL: Can we take a break for seven minutes?

MR. EVANS: Sure.

(A recess transpired.)

BY MS. SCHMAHL:

Q. Dr. Harley, would you agree with me that tuberculosis can cause scarring in the lungs?

A. Yes.

Q. Tuberculosis is an infectious disease that is not caused by smoking, correct?

A. Correct.

Q. Would you agree that histophagnosis (ph) is an infectious fungal disease?

A. Yes.

Q. And that can cause scarring in the lungs?

A. Yes.

Q. And it's not caused by smoking, correct?

A. Correct.

Q. Is it correct that pneumonia can also cause scarring of the lungs?

A. Yes.

Q. And it, too, is an infectious disease that is not caused by smoking, correct?

A. Yes.

403

Q. And occupational exposure, such as asbestos, can cause lung scarring; is that correct?

A. Correct.

Q. Silica can also cause lung scarring; is that correct?

A. Yes.

Q. There's a phenomena called scar cancers; is that correct?

A. Yes.

Q. Scar cancer is a cancer that grows out of a scar in the lung; is that correct?

A. I think scar cancer keeps being redefined, partially because of Dr. Barsky's work, but it's related to a scar in the lung. The question is whether the cancer grew from the scar or the scar grew from the cancer.

In any case, there is such an entity, and the cancer is related to the scar and grows from the outside of the scar.

Q. Would you agree that Dr. Barsky is one of the foremost authorities on scar cancers?

A. Yes.

Q. To be a true scar cancer, the scar would have to precede the cancer; is that correct?

A. It depends on the definition of scar cancer. But for a scar cancer to be a cancer that originated

404

around the edges of the scar, the scar would have to be there first.
Q. So the cancer would have to develop out of the scar instead of the scar being the result of the cancer's process; is that correct?
A. Right.
Q. So you would agree, then, that whether there are cancers that cause scars, there are also cancers that originate from scars.
A. I think there are some, yes.
Q. You noted in your expert report on the first page, second paragraph that, quote, there was a calcified spot at the top of the left lung which may have been caused by an old healed tuberculosis; do you recall that?
A. Yes.
Q. And your report also noted two small nodules in the lower part of the right lung?
A. Right.
Q. Do you have any opinion as to what those two small nodules were?
A. Maybe I'm getting tired, but I can't remember having looked at those under the microscope. If I see them under the microscope, I can tell you what they are, but I don't think I saw those.
Q. To your knowledge, was that information taken,

405

perhaps, from a radiology report or a CT scan?
A. I think it was.
Q. Do you have any knowledge as to whether those two small nodules were biopsied?
A. I don't believe they were. We had biopsies from the right lower lobe. One of them had -- the one that was described as fibrosis and pneumonia, and the other one had tumor, and I don't think either one of those was what was described in the original radiology report.
Q. And when you say "the original radiology report," are you talking about the reports from 1995, when he was originally diagnosed with cancer?
A. Right.
Q. If the calcified spot at the top of Mr. Little's left lung existed before his cancer developed, then as a matter of logic, that calcified spot was not caused by cancer; is that correct?
A. Correct.
Q. Would the calcified spot be something that would be consistent with a scar?
A. Yes.
(DFT. EXH. 36, X-ray Report dated 10/29/85, was marked for identification.)
BY MS. SCHMAHL:

406

Q. Doctor, you've just been handed what's been marked as Exhibit 36 to your deposition. For identification, Exhibit 36 is an x-ray report dated November -- dated October 29th, 1985.
Directing your attention to, there's actually only one paragraph of text, it says PA, and lateral films of the chest reveal a calcified granuloma on the left.
Do you see that?
A. I do.
Q. Is -- and this was an x-ray of Mr. Little's left chest; is that correct?
A. Correct.
Q. Is it correct that the calcified granuloma on the left may well be what you reported in your expert report as a calcified spot at the top of the left lung?
A. Probably was the same thing.
Q. And if it was -- this report is 1985, correct?
A. Right.
Q. And the x-ray report that you reference in your expert report is 1995, correct?
A. Right.
Q. So this would be ten years beforehand?
A. Correct.
Q. Are you aware, Dr. Harley, that Mr. Little has died?

407

A. Right.
Q. Do you know whether an autopsy was performed on Mr. Little or not?
A. Was not.
Q. Is there any reason that an autopsy could not have been performed on Mr. Little?
A. No.
Q. If an autopsy had been performed on Mr. Little, we would have further evidence about this possible granuloma in his left lobe; is that correct?
A. That's correct.
Q. If you or somebody here at MUSC did an autopsy on Mr. Little, you may have been able to collect additional tissue material from Mr. Little's lungs that would have helped you in your determination of lung cell type; is that correct?
A. It could have, yes.
Q. Would it be fair to say that there is no doubt that an autopsy of Mr. Little would have provided additional information about his medical condition?
A. Autopsies nearly always do and probably would have in this case.
Q. Autopsies can sometimes provide what is known as autopsy surprise; is that correct?
A. Correct.

408

Q. During your experience with autopsies, have you ever experienced autopsy surprise?
A. I've never actually called it that, but I've experienced it a number of times.
Q. For example, you find something in the autopsy that you didn't know existed before, correct?
A. Correct.
Q. Or you believed that the patient suffered from a primary condition, but upon autopsy, discovered that, in fact, another condition had resulted in that patient's death; is that correct?
A. Correct.
Q. You can, for example, on an autopsy, find a cancer that you never knew the patient had during his or her lifetime; is that correct?
A. That's right.
Q. Similarly, you can find a primary cancer that you did not know existed during that patient's lifetime; is that correct?
A. Yes.
Q. There is published medical literature that does discuss the frequency of autopsy surprise; is that correct?
A. There are a number of reports on that, yes.
Q. Based on your review of any of that medical

409

literature, do you have an opinion as to what percentage of cases result in some measure of autopsy surprise?
A. Depending on how surprised one wants to be, about a third of cases reveal significant findings that were not suspected before autopsy. And about, oh, 12 percent or so, have findings that could have changed treatment and might have resulted in the patient's survival had it been known prior to the patient's death.
Oftentimes, these occur in people who have not been sick very long. And the docs in the hospitals simply haven't had enough time to work the patients up thoroughly and would have picked up these conditions had they had more time.
But in a significant number of cases, things that are obvious at autopsy were just missed. That's always been true.
Q. Would it be fair to say that in this case, because no autopsy was performed on Mr. Little, we have no way of knowing whether his autopsy would have revealed surprises or not?
A. No, we don't know. I think the fact that he has lung cancer is clear. And the chances of his not having lung cancer at autopsy are almost nil. But there could have been any number of other things that could have been found.

410

Q. Now, in your expert disclosures, the section before, which has already been marked into evidence, you stated that one of the works that you rely on is the Dail and Hammar book; is that correct?
A. Correct.
Q. I'd like to refer you to the Dail and Hammar book Pulmonary Pathology, at page 1163. Looking in the left-hand column, I believe it is the third paragraph down, the author wrote: In this author's experience the majority of pulmonary adenocarcinomas are associated with scarring; is that correct?
A. That's true.
Q. Do you agree with that statement?
A. Yes, I think that most lung cancers of any kind are associated with some kind of scarring.
The peculiarity of so-called scar cancers is that they're usually called that when they're relatively early and small and the scarring is sort of surprisingly prominent portion of the cancer; whereas, if they were bigger and there was a lot of necrosis and then scarring and so forth, nobody would comment on it.
Q. Let me ask you--
A. Perhaps that's what he's talking to.
Q. With respect to what's written there on page 1163, what Dail and Hammar are actually talking about is

411

the phenomena of scar cancer, correct, scarring causing the cancer rather than cancer resulting in scarring; is that correct?
A. Right.
Q. And do you agree with their conclusion that the majority of pulmonary adenocarcinomas are associated with scarring?
A. Right. I think that Dr. Hammar is correct, that there is scarring in most adenocarcinomas.
Q. Would you agree that a granuloma can develop into scar tissue?
A. They nearly always do.
Q. And granulomas in a person's lung can be caused by numerous diseases, such as TB; is that correct?
A. Correct.
Q. They can also be caused by occupational exposure, such as exposure to asbestos; is that correct?
A. Not really. There really – there's not much of a granulomas component to asbestos, but there are a lot of granulomas in lung diseases that result in scarring. The very smallest granulomas might go away, but the bigger ones associated with TB, histoplasmosis, which you've mentioned; around here, heartworms, we see a modest number of those; a number of other fungal conditions; foreign body responses; sarcoidosis is a very common cause; all of

412

these things produce scars if they go on for long enough.
Q. Doctor, are you aware of any published medical literature that associates granulomas with tobacco smoke?
A. No, not directly.
Q. Did you consider the origin of Mr. Little's granuloma in your evaluation of his cancer?
A. Not really, we didn't have it, and it seemed to have been there prior to the cancer but was, I think, not toward the center of what was described as the cancer when it was removed.
Q. Did you see any --
A. Can I move this thing out of the way?
Q. Did you see any desmoplastic reaction in any of Mr. Little's tumors?
A. The first samples were small. The second ones occurred after all of that radiation and chemotherapy, which produces scarring. And desmoplasia just simply means scarring, although it implies that the scarring is a response to the cancer if you're talking about desmoplastic cancers.
But there was so much scarring caused by the radiation, that really was not possible to assess, and you couldn't relate it to the cancer.
Q. Did you see any scarring in the pre-radiation, pre-chemotherapy tumor samples?

413

A. I don't -- I didn't make any note of it, and I don't remember it.
Q. What would your criteria for scar cancer be, if you have an opinion on that?
A. Well, bearing in mind that two possibilities formed by the tumor occurred before the tumor, I think scar cancers do occur; and that in cases where there are scars in the lung from various purposes, if one sees scars with atypical hyperplasia around them and then another similar scar with a cancer appearing that arises from the edge of it, it makes sense that the tumor might have occurred at that site.
I know that tuberculosis has been associated with lung cancer in a small number of cases, it's not a very strong relationship, but it's there. The tuberculosis reaction, though, is sufficiently distinctive, that if a scar is caused by old TB or old histoplasmosis, and if the cancer arises from the edge of it, it would be remarked upon, that would be truly unusual. That's not seen that much.
Q. Would you agree that with a cancer that has a mass of 4 centimeters, that that's a fairly mature cancer?
A. That's a sizable cancer.
Q. Do you have any opinion as to how old the cancer is using principles of doubling time?

414

A. Not really; a year perhaps. There would be thoughts that if you took it back to an individual cell, that it could be a very long time.
The -- all the talk about doubling rates and how big things were and tracing them back and so forth has been very confusing in my mind. It doesn't make really good sense.
I can show you any number of cases in which the primary cancer in the lung is a small thing, sometimes too small to be detected on x-ray, and the liver weighs 3,000 grams and is full of huge tumor nodules much larger than the primary site, and obviously the lung started it all, and it was there first, so the cancer sort of chooses how fast it's going to grow.
Q. Have you noticed --
A. But the tumors -- a year -- for a 4 centimeter tumor is like that. (Indicating)
Q. About a lemon size, bigger than a golf ball?
A. It's smaller than a lemon.
Q. Okay. Bigger than a golf ball?
A. It's about a golf ball size.
Q. Okay.
A. So one, two, three, four, five years, six years. (Indicating)
But it was there when it was so small it was

415

invisible.
Q. So it may have been present, subclinically, five to six years?
A. Yeah.
Q. Given the size of the tumor at the time that it was actually diagnosed, the size of about a golf ball, would you agree that to the extent that tumor may have arisen out of a scar, that would be difficult to determine at that point in the tumor's life?
A. Because it was so big, that it had enveloped or destroyed the scar?
Q. Yes, sir.
A. It's possible. I wouldn't think it would be -- I would think it would be detectable if it were a scar cancer. That's where the idea came from, and you see them, and there's a big scar in the middle of them. I don't see any evidence of that in this case.
Q. But --
A. And I think the thing was close enough to the hilum, so it was probably around the bronchi. It was my interpretation, and you have shaken my beliefs a little bit with all of this, that it probably arose from a bronchus; that's what I thought.
Q. Sir, would you agree --
A. I can grant the possibility that it could have

416

come from scar or smaller airway, but I think it's more likely it came from a larger airway and not from a scar.
Q. Would you agree that when the left lobectomy was done on Mr. Little in March of 1996, the pathology specimen that they took, there's no way to tell whether that was taken from the core, the center of the tumor, or what exact portion of the tumor, itself, the pathology materials that you looked at came from?
A. In the larger lobectomy specimen, there are certain things I can tell. If I see normal lung and tumor next to it, I can say this is in the periphery. If it's all tumor, I can say that's it's inside the tumor. Beyond that, I couldn't really say, just from looking at the slides.
Q. Right. So it would not be possible, unless the pathologist had identified it as being a slide taken from the exact center of the tumor, you couldn't tell, by looking at it under the microscope, whether it did come from the center of the tumor or not; is that correct?
A. That's correct. And all I could say is that it was inside the tumor somewhere.
Q. If Mr. Little had a history of scarring in his lungs, would that affect your opinion in any way as to causation or cell type?
A. Well, he did have some little scars. I don't

417

think they had anything to do with this tumor. So I guess the answer is that didn't affect my opinion.
Q. Are you familiar with the term "de-differentiation"?
A. Yes.
Q. What does that term mean?
A. That in terms of a cancer that is well or better differentiated and looked more like the tissue from which it came at a given time, it changed so that it did not look so much like that, and finally to the point that it might not have looked like it all. It's appearance of the individual cells and of the pattern of growth would have changed and become less well-differentiated than it was originally.
Q. Would you agree that a younger tumor may well have more clearly-defined cells?
A. Smaller tumors and earlier tumors frequently do, yes.
Q. And as the tumor matures and ages and there's necrosis and continuing mutations, that that tumor may become increasingly more poorly-differentiated?
A. That does happen, usually as a response to therapy, but it can also happen spontaneously.
(DFT. EXH. 37, Surgical Pathology Report dated 2/9/99, was marked for

418

identification.)
BY MS. SCHMAHL:
Q. Okay. You've just been handed what has been marked as Exhibit 37 to your deposition. For identification, Exhibit 37 is a cytopathology report dated February 9th, 1999.
According to Exhibit 37, you were the consulting pathologist for Mr. Little's February 9th diagnosis; is that correct?
A. Am I missing something here?
Q. I think you are.
A. All I see here is John Metcalf.
MS. SCHMAHL: For the record, what had been marked as Defendant's Exhibit 37 was the incorrect document and has been withdrawn and replaced.
Defendant's Exhibit 37 is now a surgical pathology report dated February 9, 1999.
BY MS. SCHMAHL:
Q. Dr. Harley, you were the consulting pathologist on Mr. Harley's (sic) February 9th pathology report; is that correct?
A. Mr. Little's report, yes. Now, this is from 2-9-99.
Q. Right. And in this 2-9-99 surgical pathology report, your diagnosis was that it was a non-small

419

carcinoma, poorly-differentiated; is that correct?
A. Correct.
Q. Would this be an example of de-differentiation, where when you looked at Mr. Little's earlier tumor samples, you had diagnosed them as large cell, but here in February of 1999, your diagnosis was simply poorly-differentiated non-small cell?
A. There could be a component of that. More likely, this is simply a matter of having a very small specimen. These are transbronchial biopsies, and by their nature, extremely limited. Each one of them about, well, smaller than a match head, so they're really tiny.
Q. Do you recall or do you have any opinion as to whether Mr. Little's February 1999 pathology materials were less well-differentiated than his March or September 1996 materials?
A. No, I don't remember, and I think it would be hard to say with small specimens like this, depending on how lucky one happened to be with the biopsy.
Q. Would you expect to see more or less de-differentiation in a primary lung cancer that had already metastasized?
A. Well, if it's metastasized, it tends to be later. And so if there's going to be any de-differentiation, it would tend to occur in such tumors,

420

but I think therapy is a bigger factor in whether they do that, in my experience.

Q. How does de-differentiation relate to heterogeneity, if at all?

A. Of the tumor?

Q. Yes.

A. They could be related. In what sense are you referring to heterogeneity? Are you talking about the way the tumor cells grow in one place versus another?

Q. Well, why don't you give it whatever definition you want, and then tell me what, if anything -- what, if any, relationship that would have to de-differentiation?

A. Heterogenous is opposite from homogenous. Homogenous is everything's the same. Heterogenous is everything is different.

In the case of cancers, there can be tumors that have totally different appearances, sometimes within the same microscopic field. So there's an adenocarcinoma here, something that looks squamoid over here, something that's solid over here, maybe a little bone production over here, so they do a lot of different things. One could actually look at that as being a manifestation of differentiation.

But if, for instance, the tumor were an adenocarcinoma and made glands and then stopped doing

421

that, that part of the tumor would look like the solid component, and this is very confusing, but de-differentiation, total de-differentiation would result in a more homogenous pattern rather than a heterogenous pattern.

On the other hand, de-differentiation implies change in the tumor and the tumor could decide to change and start producing different patterns. I've seen them do that.

So, actually, I guess, it could go either way.

Q. I would like to, hopefully very briefly, discuss some of the diagnostic criteria for BAC with you. I know it's getting late and everyone would like to wrap this up. What are the Air Force Institute of Pathology, the AFIP criteria for determining whether a cancer is a BAC?

A. I think the major feature is the lipidic growth pattern, wherein it grows along alveolar walls without destruction of the wall.

Q. Are there any other diagnostic criteria that you are aware that the AFIP uses for BAC?

A. I think it is allowed to have a scar, if it's a single small nodule, and allowed to grow into the scar, so long as it doesn't grow into normal lung tissues around the outside; for instance, across the connective tissue septa, through the wall of the bronchus or through the

422

pleura; and the tumor should have only the lipidic growth pattern. Lots of lung cancers are adenocarcinomas with some focal features of BAC.

The stringency with which the criteria are applied vary from one pathologist to another.

Q. Does the AFIP criteria for diagnosing BAC, would it exclude as a BAC any tumor that had metastasized?

A. The new definitions would suggest that it should be localized to the lung.

Q. My question is --

A. However, it's not used that way; it never has been. The BAC is the appearance of this lipidic growth pattern in the lung. If it's in a lymph node, I think most pathologists would still say that's a BAC; it has metastasized to the lymph node.

Q. So you do not follow the strict 1999 WHO classification that now would exclude any metastatic tumor from being a BAC; is that correct?

A. No. For purposes of classifying these now and putting them in a tumor registry and trying to comply with what they're trying to do, which is to show the -- a large difference in behavior, if these criteria are adhered to, I am trying to do that, and if I feel like the picture is incomplete, I use their terms, and then explain it in a footnote.

423

Q. So you --

A. And I'm using the term "adenocarcinoma with bronchioloalveolar features" very commonly now; whereas, I didn't before.

Q. Doctor, would you agree that a peripheral pleura-based tumor is one indicator of BAC?

A. Right, they are, at least my definition, peripheral.

Q. That a tumor that manifests a well-differentiated adeno-carco (ph) tenacious infiltration pattern with an intact intersticial framework of the lung with no evidence of a primary adenocarcinoma at some extra pulmonary site and pleural puckering would be consistent with a BAC?

A. Yes.

Q. In order for a cancer to be a BAC, does it have to be homogeneous throughout the tumor?

A. It has to be fairly homogeneous in its growth pattern. It can't be extremely papillary. It can't grow in a solid pattern to a great degree. It has to grow along the alveolar walls and essentially nothing else.

Q. Would you agree that BACs can be heterogeneous?

A. Heterogeneous?

Q. Yes, sir.

A. They can be, to some extent.

424

Now, there's a big question as to whether the multiple fossae that are characteristic of BAC are metastases or whether they're individual primary tumors. And there is some fairly high-power recent literature suggesting both sides of that issue.

So to my way of thinking, it's still not settled, although it apparently can have multiple fossae of development or it can spread through airways and implant itself and grow. I think it seems to be capable of doing both things.

Q. Would you agree that a BAC can de-differentiate?

A. Yes.

Q. I just want to clarify what you said a few minutes ago. You are currently using the 1999 WHO Classification for Tumor Registry; is that correct?

A. Right. I'm also -- since I'm putting these in the tumor registry from material here, I personally try to use those criteria for any diagnosis. Other people aren't quite so strict about that as I am.

Q. Do you have any opinion as to whether the new diagnostic criteria for BAC, does that implicate the validity of epidemiological studies that used an older diagnostic criteria, such as the AFIP?

A. The differences between the new WHO and the older, but relatively recent, AFIP fascicle are not great.

425

They're pretty nearly the same, but there are, I think, clearly implications, in that the stricter the criteria, the fewer tumors fit those criteria.

And the -- in a case of 100 lung cancers, the fewer BACs would be accepted. The -- if you permit the term cruder of the criteria, the looser the criteria, the more adenocarcinomas with bronchioalveolar features are included; that is, more things that are more ordinary adenocarcinomas that grow a little bit like a BAC.

And some of this could explain the relatively huge differences in incidence of BACs in various collections in various places, but some of it is sort of beyond my ability to explain.

I don't understand how Dr. Barsky can have 24 percent BACs, and other people are down at the 9 or 10 percent range. But he's talking about women, mostly; he's in a different part of the country. I'm not sure. But it is possible to have quite a range of things that one calls BAC, depending on how strict the criteria are.

Q. And would you agree that all of the epidemiological studies done to date, that none of them would have used the 1999 WHO criteria?

A. That's correct.

Q. At this point in time, with the state of current medical literature, have any studies been published that

426

would contradict earlier epidemiological studies that used looser criteria for what constituted BAC?

A. I haven't seen any.

Q. And that's the purpose of, for example, the tumor registry that you're doing now, is that correct, to see whether a more stringent standard or diagnostic criteria for BAC will reveal additional information about the course of treatment, causation, and things of that nature; is that correct?

A. It can be used for that. It's mostly just to have readily available a variety of different types of tumors for genetic studies and things of that nature.

Q. But at this point, the process is new enough that the jury's just not in on that; is that correct?

A. Right. However, I would point out that few, if any, prior studies would have called Mr. Little's cancer a BAC.

I think the fact that we have several different pathologists, including the ones that saw this originally at MUSC, you know, not even thinking of BAC, to support that notion, that nobody would have called this a BAC --

Q. Because --

A. -- in any of the older studies.

Q. Because, in your opinion at least, Mr. Little's cancer would not have met the definition of even an

427

earlier diagnostic criteria?

A. It doesn't look a thing like one, it doesn't grow alveolar walls in a lipidic fashion, so nobody would have looked at this and said, oh, look at the BAC.

Q. But is it fair to say that equally competent pathologists can look at same slides and come to different conclusions?

A. They do. They seem to be doing that here.

Q. And competent pathologists can have an honest, intellectual dispute about what they see under the microscope; is that correct?

A. They do. There's not much dispute about this, but somebody with the experience that Dr. Barsky has is somebody that I think we'd have to pay careful attention to. On the other hand, he's seen maybe so many BACs that he sees more of them than some other people would, maybe he sees patterns that we don't normally see.

Q. Irrespective, for example, you and Dr. Roggli saw large cell; is that correct?

A. Right.

Q. And Dr. Hammar saw what he thought could be an adenosquamous; is that correct?

A. I think he saw several different patterns, but he didn't see a BAC.

Q. And the treating pathologist originally saw

squamous cancer, right, or what they believed to be a squamous cancer?
A. Right.
Q. And later on, other pathologists, including yourself, had looked at it and seen a poorly-differentiated carcinoma; is that correct?
A. Right.
Q. So you wouldn't ascribe any sinister motive to seeing a different type of cancer, would you?
A. No.
MS. SCHMAHL: If I can have just a couple seconds to look through, just to make sure I - didn't skip anything huge. I think we'll just need to mark the slides, and then I'll be done.
Do you want to conform the slides, or is it late enough? Are you tired?
MR. EVANS: I actually marked mine at lunchtime.
MS. SCHMAHL: You don't need to put that on the record.
(Off-the-record conference.)
(DFT. EXH. 38, Twenty-three Slides, was marked for identification.)
(DFT. EXH. 39, Twenty-four Photographs of the 23 Slides, was marked for identification.)
MS. SCHMAHL: For the record, we are going to mark into evidence as Exhibit 38, 23 slides that correspond to the slides that Dr. Harley had discussed during his deposition. We will have slides one through 17 with actually two copies of slide 4 for a total of 18 slides, and then we'll have slides 18-1 through 18-5 for a grand total of 23 slides. The slides will be retained by counsel for R.J. Reynolds.
As Exhibit 39, we are marking into evidence photographs which are copies of the photomicrographs that have already been marked into evidence as Exhibit 38.
There are a total of 24 photographs which correspond to the 23 photomicrographs, plus the extra copy of slide number 1 which was returned to Dr. Harley.
So in this set, we should have two copies of slide number 1 and two copies of slide number 4.
Jerry, that's all I have.
The exhibit will be retained by counsel for R.J. Reynolds.
MR. EVANS: And I have no questions at this time.

(The deposition concluded at 5:18 p.m.)

CERTIFICATE OF REPORTER

I, Madonna M. Farrell, Registered Professional Reporter and Notary Public in and for the State of South Carolina do hereby certify that the deponent, RUSSELL A. HARLEY, M.D., was duly sworn by me to testify to the truth, and that the above deposition, pages 228 through 430, inclusive, was recorded stenographically by me and transcribed through computer-aided transcription by me to the best of my ability.

I FURTHER CERTIFY that the foregoing transcript is a true and correct transcript of the testimony given by the said witness at the time and place specified.

I FURTHER CERTIFY that I am neither attorney or counsel for, nor related to or employed by any of the parties to the action in which this deposition is taken, or financially interested in this action.

IN WITNESS WHEREOF, I have set my hand and seal this 3rd day of June, 2000.

_____
Madonna M. Farrell
Registered Professional Reporter
Notary Public
My commission expires
October 20, 2005

VERIFICATION OF DEPONENT

I, RUSSELL A. HARLEY, M.D., have read the foregoing deposition consisting of 204 pages which was reported by Madonna M. Farrell, Registered Professional Reporter and notary public in and for the State of South Carolina on May 23, 2000.

I find the transcript of this deposition to be a true and accurate transcript according to my testimony on that date with the exception of ___ corrections as listed on the attached correction sheet, which was filled in by me.

_____
RUSSELL A. HARLEY, M.D.

_____, 2000

ERRATA PAGE

PAGE # - LINE # CHANGE AND/OR CORRECTION (AND EXPLANATION)

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THE ABOVE CHANGES WERE NOTED BY ME ON THIS ERRATA PAGE BEFORE SIGNING THE ATTACHED VERIFICATION OF DEPONENT. I HAVE RETAINED A COPY OF THIS ERRATA PAGE FOR MY RECORDS, AND THE COURT REPORTER IS TO ATTACH THIS PAGE AND MY VERIFICATION TO THE ORIGINAL TRANSCRIPT.

DATED: ___ _____
RUSSELL A. HARLEY, M.D.

INDEX

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Page

(No Information Requested)

EXHIBITS

Page

EXHIBITS

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